```
                                                      ENTRY     SESSION
FULL ESTIMATED COST                                    0.63        0.63

FILE 'REGISTRY' ENTERED AT 09:14:23 ON 17 MAY 2004
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   16 MAY 2004  HIGHEST RN 682330-24-1
DICTIONARY FILE UPDATES:  16 MAY 2004  HIGHEST RN 682330-24-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\STNEXP4\QUERIES\184a.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 09:18:04 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     82 TO ITERATE

100.0% PROCESSED      82 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          1097 TO     2183
PROJECTED ANSWERS:                0 TO        0

L2            0 SEA SSS SAM L1

=> search l1
ENTER TYPE OF SEARCH (SSS), CSS, FAMILY, OR EXACT:.
ENTER SCOPE OF SEARCH (SAMPLE), FULL, RANGE, OR SUBSET:full
FULL SEARCH INITIATED 09:18:13 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   2088 TO ITERATE
```
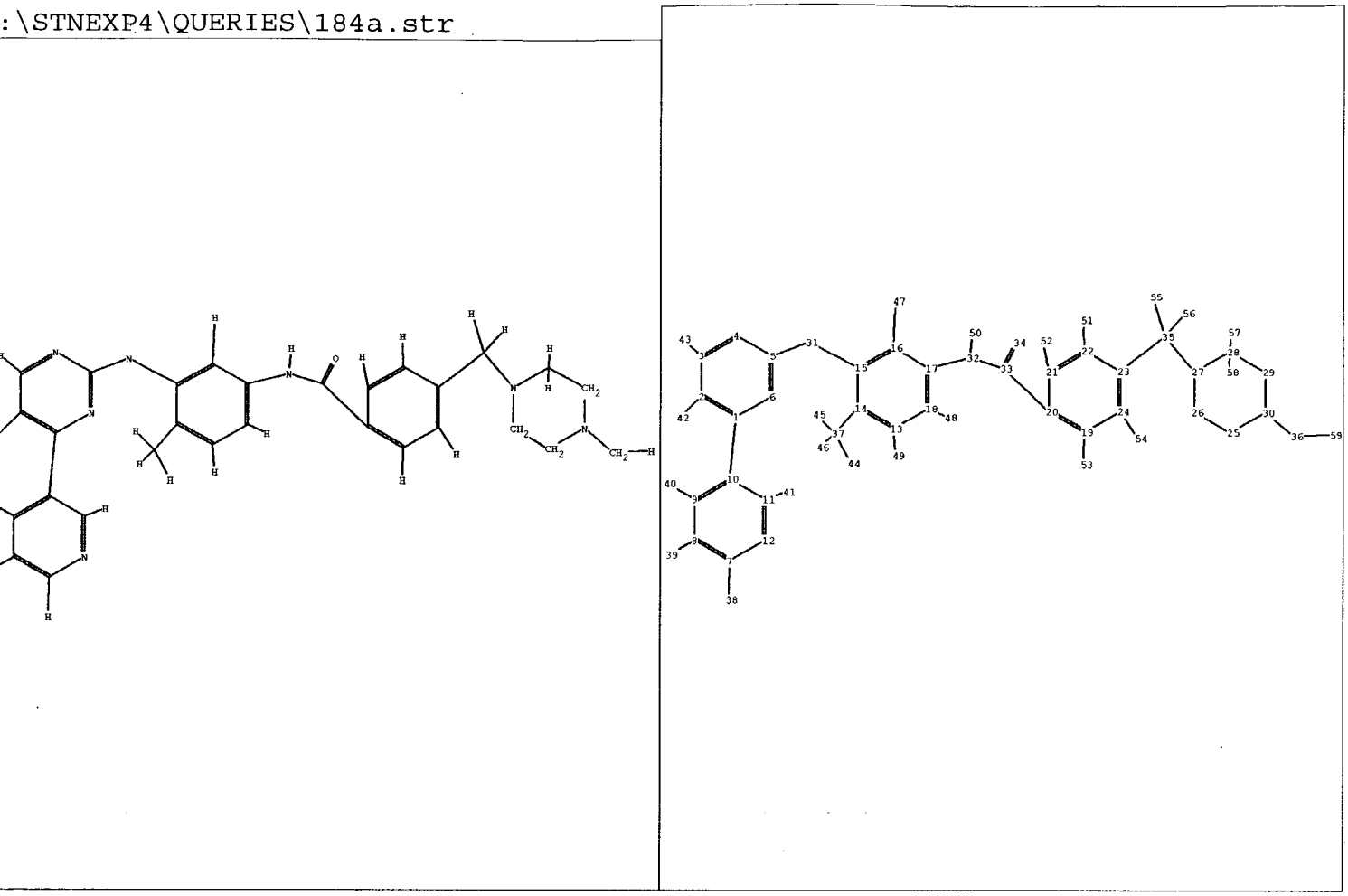

:\STNEXP4\QUERIES\184a.str



hain nodes :
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48
49 50 51 52 53 54 55 56 57 58 59
ing nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
21 22 23 24 25 26 27 28 29 30
hain bonds :
1-10 2-42 3-43 5-31 7-38 8-39 9-40 11-41 13-49 14-37 15-31
16-47 17-32 18-48 19-53 20-33 21-52 22-51 23-35 24-54 27-35
28-57 28-58 30-36 32-33 32-50 33-34 35-55 35-56 36-59 37-44
37-45 37-46
ing bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14
13-18 14-15 15-16 16-17 17-18 19-20 19-24 20-21 21-22 22-23
23-24 25-26 25-30 26-27 27-28 28-29 29-30
xact/norm bonds :
5-31 15-31 17-32 25-26 25-30 26-27 27-28 27-35 28-29 29-30
32-33 33-34
xact bonds :
1-10 2-42 3-43 7-38 8-39 9-40 11-41 13-49 14-37 16-47 18-48
19-53 20-33 21-52 22-51 23-35 24-54 28-57 28-58 30-36 32-50
35-55 35-56 36-59 37-44 37-45 37-46
ormalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 13-14
13-18 14-15 15-16 16-17 17-18 19-20 19-24 20-21 21-22 22-23
23-24

atch level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom
10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom
18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom
26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:CLASS 32:CLASS
33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS
40:CLASS 41:CLASS 42:CLASS 43:CLASS 44:CLASS 45:CLASS 46:CLASS
47:CLASS 48:CLASS 49:CLASS 50:CLASS 51:CLASS 52:CLASS 53:CLASS
54:CLASS 55:CLASS 56:CLASS 57:CLASS 58:CLASS 59:CLASS

Welcome to STN International! Enter x:x

LOGINID:sssptau129pxo

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 5	FEB 05	German (DE) application and patent publication number format changes
NEWS 6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 8	MAR 03	FRANCEPAT now available on STN
NEWS 9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS 10	MAR 29	WPIFV now available on STN
NEWS 11	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 12	APR 26	PROMT: New display field available
NEWS 13	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS 14	APR 26	LITALERT now available on STN
NEWS 15	APR 27	NLDB: New search and display fields available
NEWS 16	May 10	PROUSDDR now available on STN
NEWS 17	May 19	PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS 18	May 12	EXTEND option available in structure searching
NEWS 19	May 12	Polymer links for the POLYLINK command completed in REGISTRY

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:12:52 ON 17 MAY 2004

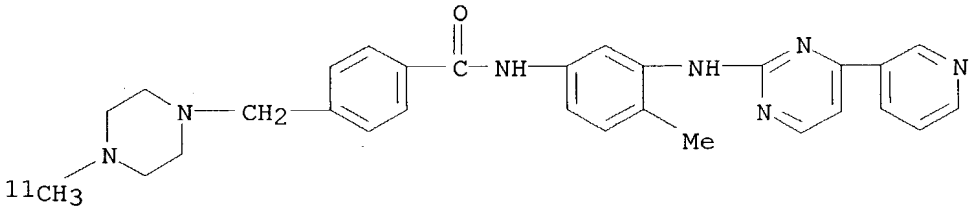
=> file reg
COST IN U.S. DOLLARS SINCE FILE TOTAL

100.0% PROCESSED 2088 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

L3 8 SEA SSS FUL L1

=> d l3 1-8

L3 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
RN 616193-60-3 REGISTRY
CN Benzamide, 4-[[4-(methyl-11C)-1-piperazinyl]methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C29 H31 N7 O
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

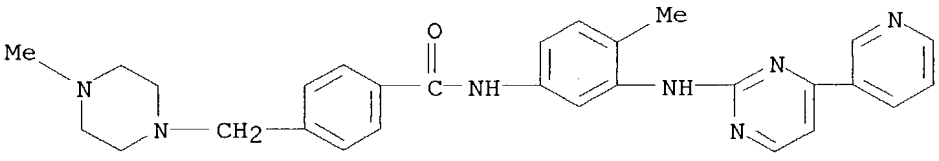


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
RN 586350-83-6 REGISTRY
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, nitrate (9CI) (CA INDEX NAME)
MF C29 H31 N7 O . x H N O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

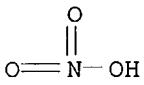
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



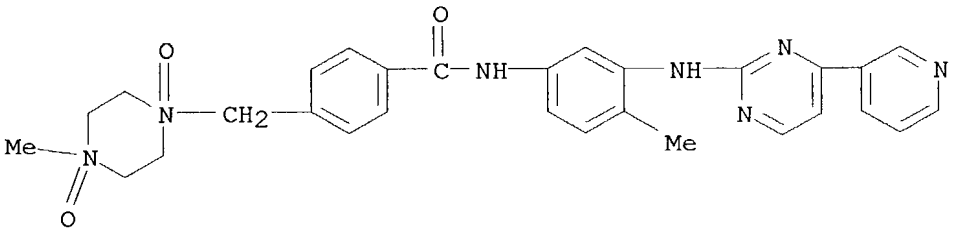
CM 2

CRN 7697-37-2
CMF H N O3



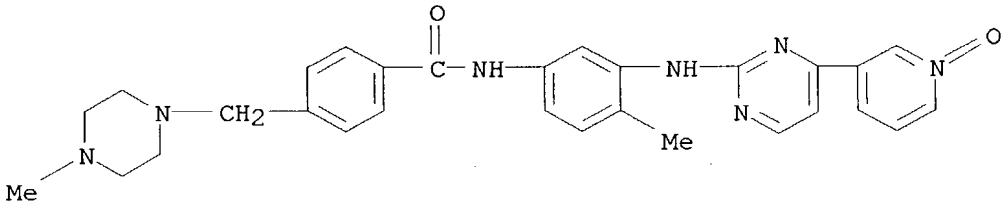
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
RN 571186-93-1 REGISTRY
CN Benzamide, 4-[(4-methyl-1,4-dioxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C29 H31 N7 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
RN 571186-92-0 REGISTRY
CN Benzamide, N-[4-methyl-3-[[4-(1-oxido-3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-4-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C29 H31 N7 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

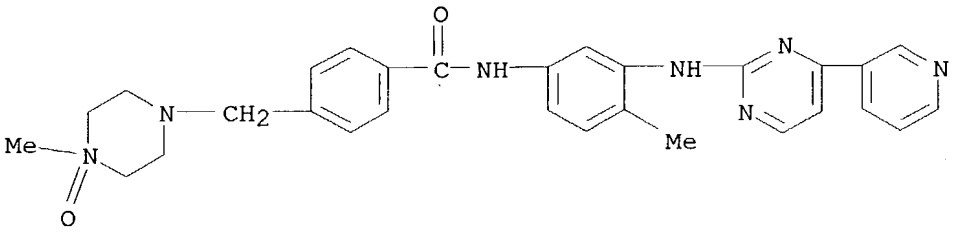


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
RN 571186-91-9 REGISTRY

CN Benzamide, 4-[(4-methyl-4-oxido-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C29 H31 N7 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

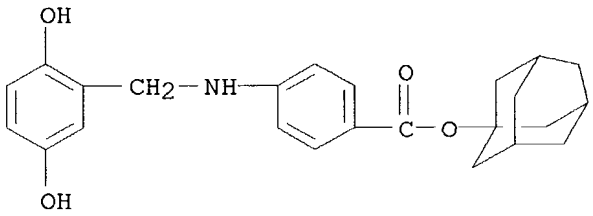


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
RN 518355-21-0 REGISTRY
CN Benzoic acid, 4-[[(2,5-dihydroxyphenyl)methyl]amino]-, tricyclo[3.3.1.13,7]dec-1-yl ester, mixt. with 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]benzamide (9CI) (CA INDEX NAME)
MF C29 H31 N7 O . C24 H27 N O4
CI MXS
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

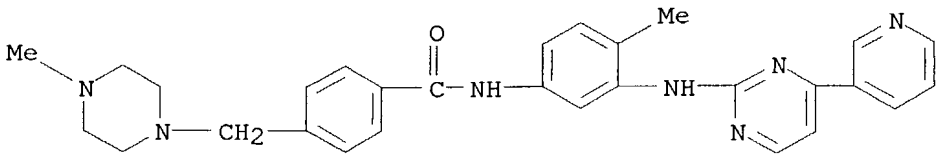
CM 1

CRN 241127-58-2
CMF C24 H27 N O4



CM 2

CRN 152459-95-5
CMF C29 H31 N7 O

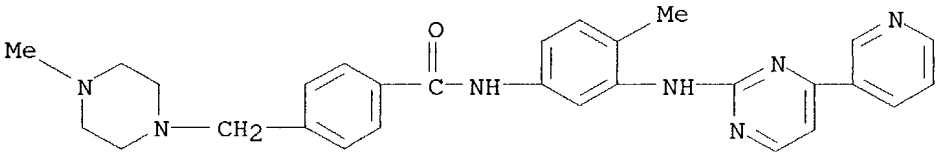


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
RN 220127-57-1 REGISTRY
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN CGP 57148B
CN Gleevac
CN Gleevec
CN Glivec
CN Imatinib mesilate
CN Imatinib mesylate
CN STI 571
MF C29 H31 N7 O . C H4 O3 S
SR CA
LC STN Files: ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS, EMBASE, HSDB*, IMSPATENTS, IMSRESEARCH, MRCK*, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

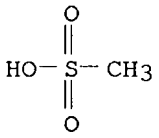
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



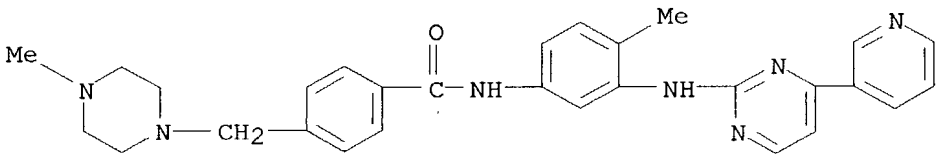
CM 2

CRN 75-75-2
CMF C H4 O3 S



568 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
578 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2004 ACS on STN
RN 152459-95-5 REGISTRY
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN CGP 57148
CN Imatinib
MF C29 H31 N7 O
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CIN, DDFU, DIOGENES, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, SYNTHLINE, TOXCENTER, USAN, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

175 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
182 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s 220127-57-1/rn
L4 1 220127-57-1/RN

=> s 152459-95-5/rn
L5 1 152459-95-5/RN

=> d his

(FILE 'HOME' ENTERED AT 09:12:52 ON 17 MAY 2004)

FILE 'REGISTRY' ENTERED AT 09:14:23 ON 17 MAY 2004
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 8 SEARCH L1 FULL
L4 1 S 220127-57-1/RN
L5 1 S 152459-95-5/RN

=> sl3 not l4
SL3 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

```
=> s l3 not l4
L6            7 L3 NOT L4

=> s l6 not l5
L7            6 L6 NOT L5

=> file caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       174.62     175.25

FILE 'CAPLUS' ENTERED AT 09:22:01 ON 17 MAY 2004
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FILE COVERS 1907 - 17 May 2004  VOL 140 ISS 21
FILE LAST UPDATED: 16 May 2004  (20040516/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s restinosis
L8           10 RESTINOSIS

=> s atherosclerosis or heart or cardio or stent or artereosclerosis or
cardiovascular or stroke or infarct or circulatory or artery
         39336 ATHEROSCLEROSIS
        287906 HEART
          1777 CARDIO
          1886 STENT
             3 ARTEREOSCLEROSIS
         64214 CARDIOVASCULAR
         21412 STROKE
          6776 INFARCT
         17341 CIRCULATORY
        108621 ARTERY
L9      446480 ATHEROSCLEROSIS OR HEART OR CARDIO OR STENT OR ARTEREOSCLEROSIS
               OR CARDIOVASCULAR OR STROKE OR INFARCT OR CIRCULATORY OR ARTERY

=> s arteries or thrombosis or thrombotic or platelet or cardiac
         30223 ARTERIES
         18084 THROMBOSIS
          5121 THROMBOTIC
         93037 PLATELET
         99735 CARDIAC
```

```
L10     231866 ARTERIES OR THROMBOSIS OR THROMBOTIC OR PLATELET OR CARDIAC

=> s l9 or l10
L11     558207 L9 OR L10

=> d his

     (FILE 'HOME' ENTERED AT 09:12:52 ON 17 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 09:14:23 ON 17 MAY 2004
L1              STRUCTURE UPLOADED
L2            0 S L1
L3            8 SEARCH L1 FULL
L4            1 S 220127-57-1/RN
L5            1 S 152459-95-5/RN
L6            7 S L3 NOT L4
L7            6 S L6 NOT L5

     FILE 'CAPLUS' ENTERED AT 09:22:01 ON 17 MAY 2004
L8           10 S RESTINOSIS
L9       446480 S ATHEROSCLEROSIS OR HEART OR CARDIO OR STENT OR ARTEREOSCLEROS
L10      231866 S ARTERIES OR THROMBOSIS OR THROMBOTIC OR PLATELET OR CARDIAC
L11      558207 S L9 OR L10

=> s l3 and l8
           725 L3
L12          0 L3 AND L8

=> s ;4
ENTER LOGIC EXPRESSION, QUERY NAME, OR (END):emd
L13       1362 EMD


4 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:n

=> s l4
L14         577 L4

=> s l5
L15         182 L5

=> s l7
L16           4 L7

=> s l14 and l11
L17         106 L14 AND L11

=> s l15 and l11
L18          35 L15 AND L11

=> s l16 and l11
L19           0 L16 AND L11
```

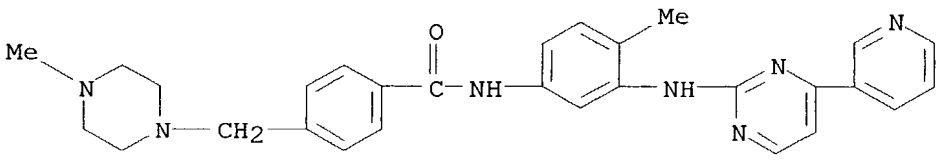
=> s l17 and l18
L20 6 L17 AND L18

=> d l20 1-6 fbib ab hitstr

L20 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:331787 CAPLUS
TI Treatment of tuberous sclerosis associated neoplasms with **platelet** -derived growth factor receptor tyrosine kinase or bcr-abl tyrosine kinase inhibitors, especially N-phenyl-2-pyrimidineamines
IN Arbiser, Jack
PA USA
SO U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

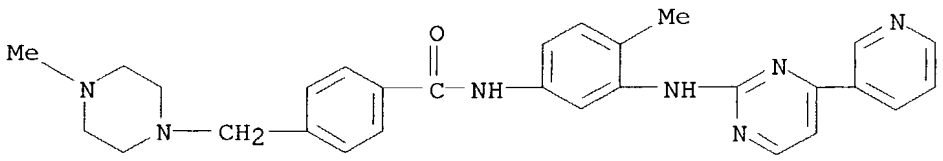
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004077661	A1	20040422	US 2003-655407	20030904
			US 2002-408550PP	20020905

AB The present invention relates to the use of PDGF receptor tyrosine kinase or bcr-abl tyrosine kinase inhibitors, especially of N-phenyl-2-pyrimidine-amine derivs. I (R1 = 4-pyrazinyl, 1-methyl-1H-pyrrolyl, etc.; R2, R3 = H, lower alkyl; R4-8 = nitro, fluoro-substituted lower alkoxy, -N(R9)-C(=X)-(Y)nR10; R9 = H, lower alkyl; X = oxo, thio, imino, N-lower alkylimino, hydroximino, or O-lower alkyl-hydroximino; Y = O, NH; n = 0 or 1; R10 = C5 aliphatic radical, aromatic, etc.) or in pharmaceutically acceptable salt form, in the manufacture of a pharmaceutical composition for the treatment of tuberous sclerosis associated neoplasms; to a method of treatment of warm-blooded animals, including humans, suffering from a tuberous sclerosis associated neoplasms. Cells of SV7tert, a cell line derived from a human angiomyolipoma, were inhibited by 4-(4-methyl-1-piperazin-1-ylmethyl)-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]benzamide.
IT **152459-95-5 152459-95-5D**, acceptable salts
220127-57-1
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tuberous sclerosis-associated neoplasms treatment with **platelet** -derived growth factor receptor tyrosine kinase or bcr-abl tyrosine kinase inhibitors, especially N-Ph-2-pyrimidineamines)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-

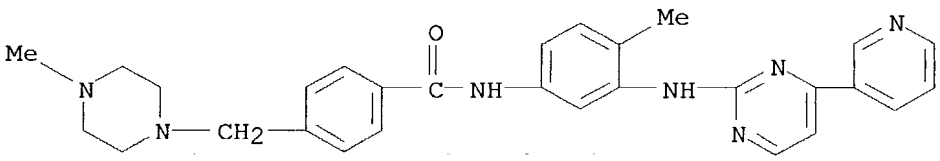
pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

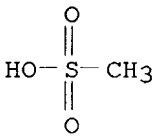
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L20 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:912990 CAPLUS
DN 139:375014
TI Methods and compositions with N-phenyl-2-pyrimidine compounds inhibiting **platelet** derived growth factor receptor for the treatment of graft failure
IN Sukhatme, Vikas P.
PA Beth Israel Deaconess Medical Center, USA
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 2003094904	A1	20031120	WO 2003-US14916	20030513

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-380180PP 20020513
US 2003-464023PP 20030418

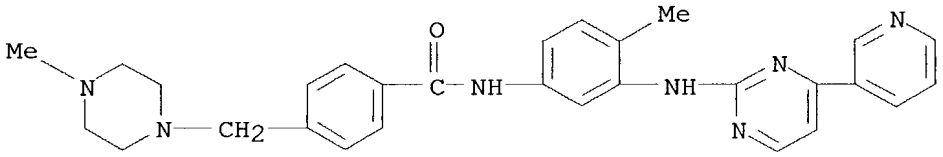
OS MARPAT 139:375014

AB The present invention provides methods and compns. for treating graft failure resulting from neointimal hyperplasia. These methods and compns. feature the use of **platelet** derived growth factor receptor (PDGFR) inhibitor compds., such as N-phenyl-2-pyrimidine compds. (e.g., imatinib mesylate) to inhibit the biol. activity of the PDGFR and treat AV graft failure. Gleevec and rapamycin inhibited smooth muscle cell migration.

IT **152459-95-5 220127-57-1**, Imatinib mesylate
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-Ph-2-pyrimidine compds. inhibiting **platelet** derived growth factor receptor for treatment of graft failure)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)

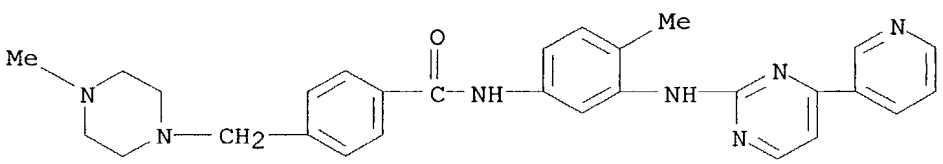


RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

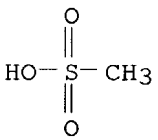
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

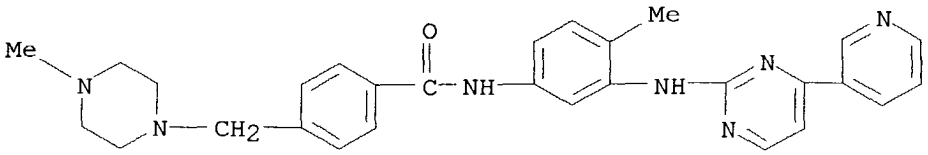
L20 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:875113 CAPLUS
DN 139:345924
TI PDGF receptor tyrosine kinase inhibitors for the treatment of polycythemia vera
IN Kantarjian, Hagop
PA Board of Regents, the University of Texas System, USA
SO PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003090750	A1	20031106	WO 2003-IB1632	20030422

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

US 2002-375143PP 20020424

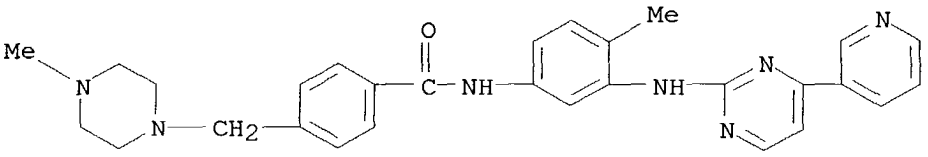
AB The invention discloses the treatment of polycythemia vera by administration of N-[5-(4-(4-methylpiperazinomethyl)benzoylamido)-2-methylphenyl]-4-(3-pyridyl)-2-pyrimidineamine or 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-((4-(3-pyridinyl)-2-pyrimidinyl)amino)phenyl]benzamide in free form or in pharmaceutically acceptable salt form.
IT **152459-95-5 220127-57-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PDGF receptor tyrosine kinase inhibitors for treatment of polycythemia vera)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

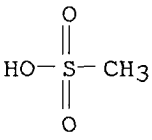
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:757504 CAPLUS
DN 139:271054
TI Imatinib for treating angiotensin II-mediated diseases
IN Gilbert, Richard Ernest; Kelly, Darren James; Feldman, David Louis
PA Novartis A.-G., Switz.; The University of Melbourne
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003077892	A2	20030925	WO 2003-EP2709	20030314
	WO 2003077892	A3	20031224		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

GB 2002-6216 A 20020315
GB 2002-6217 A 20020315
GB 2002-17505 A 20020729

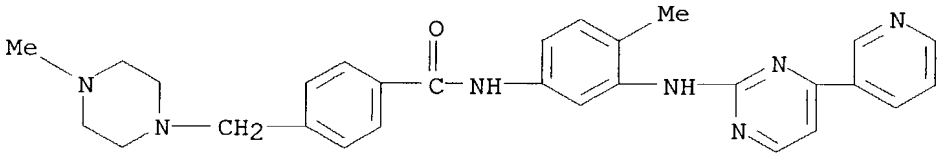
OS MARPAT 139:271054

AB A PDGF receptor tyrosine kinase inhibitor, especially 4-(4-methylpiperazin-1-ylmethyl)-N-[[4-methyl-3-(4-pyridin-3-yl)pyrimidin-2-ylamino]phenyl]benzamide (I) or a pharmaceutically acceptable salt can be used in the treatment of angiotensin II-induced diseases and a combination which comprises (a) a PDGF receptor tyrosine kinase inhibitor, an antihypertensive, an aldosterone antagonist, an aldosterone synthase inhibitor and/or an angiotensin receptor blocker agent and optionally at least one pharmaceutically acceptable carrier for simultaneous, sep. or sequential use, in particular for the treatment of hypertension and hypertension-induced diseases. Imatini9b had no effect on systolic blood pressure but significantly reduced mesenteric weight in animals receiving angiotensin II. Pharmaceutical formulations of Imatinib were given.

IT **152459-95-5**, Imatinib **220127-57-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Imatinib for treating angiotensin II-mediated diseases)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)

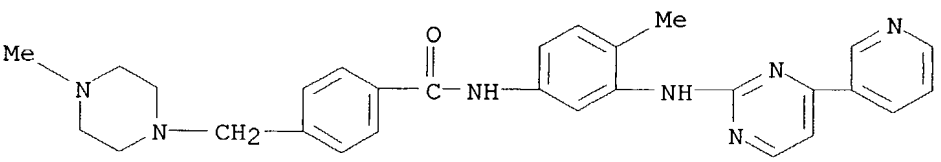


RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

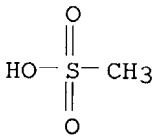
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L20 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:551338 CAPLUS
DN 139:111702
TI Compositions and methods using ATP-dependent γ-secretase modulators for prevention and treatment of amyloid-β peptide-related disorders, and screening methods for modulators of Aβ
IN Netzer, William J.; Greengard, Paul; Xu, Huaxi
PA The Rockefeller University, USA
SO PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003057165	A2	20030717	WO 2003-US249	20030106
	WO 2003057165	A3	20031113		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

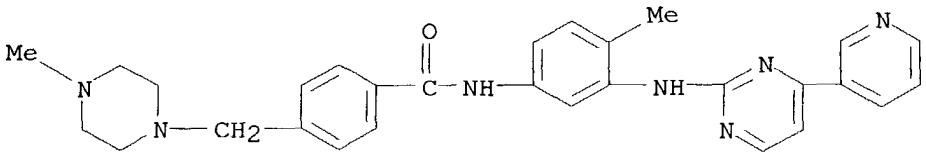
				US 2002-345009PP	20020104
	US 2004028673	A1	20040212	US 2003-337261	20030106
				US 2002-345009PP	20020104

OS MARPAT 139:111702
AB The invention provides methods and compns. for modulating levels of amyloid-β peptide (Aβ) exhibited by cells or tissues. The invention also provides pharmaceutical compns. and methods of screening for compds. that modulate Aβ levels. The invention also provides modulation of Aβ levels via selective modulation (e.g., inhibition) of ATP-dependent γ-secretase activity. The invention also provides methods of preventing, treating or ameliorating the symptoms of a disorder, including but not limited to an Aβ-related disorder, by administering a modulator of γ-secretase, including, but not limited to, a selective inhibitor of ATP-dependent γ-secretase activity or an agent that decreases the formation of active (or optimally active) γ-secretase. The invention also provides the use of inhibitors of

ATP-dependent γ-secretase activity to prevent, treat or ameliorate the symptoms of Alzheimer's disease.

IT **152459-95-5D**, derivs. **220127-57-1**, STI 571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ATP-dependent enzyme modulators for prevention and treatment of amyloid-β peptide-related disorders, and screening methods for modulators of Aβ)

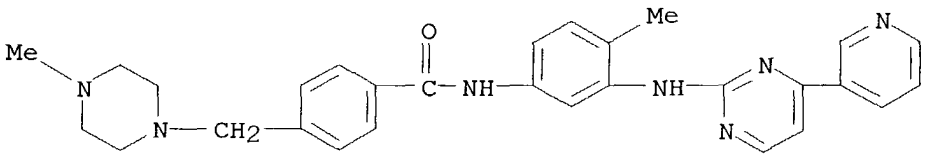
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

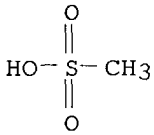
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L20 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:413877 CAPLUS
DN 138:396218
TI Combination for the treatment of endothelial damage

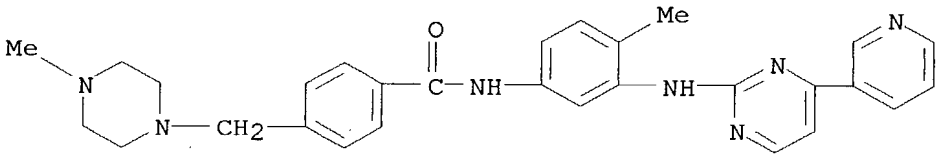
IN Alitalo, Kari; Heldin, Carl Henrik; Leppanen, Olli; Ostman, Arne; Yla-Herttuala, Seppo
PA Finland
SO U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003099687	A1	20030529	US 2002-227081	20020823
			GB 2001-20690 A	20010824

AB The invention relates to a combination of (a) an inhibitor of **platelet**-derived growth factor (PDGF) activity and (b) a vector for vascular endothelial growth factor (VEGF-, especially VEGF-C) gene transfer, a pharmaceutical preparation comprising (a) and (b) in combination together with a pharmaceutically acceptable carrier material; a product comprising (a) and (b) as defined above and optionally a pharmaceutically acceptable carrier material, for simultaneous, chronol. staggered or sep. use; a method of administering or the use of said combination or product for the treatment of endothelial damage; and/or to the use of (a) and (b) for the manufacture of said pharmaceutical preparation or product for the treatment of endothelial damage.

IT **152459-95-5 220127-57-1**, STI571
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination for treatment of vascular endothelial damage using **platelet**-derived growth factor inhibitors and gene transfer of vascular endothelial growth factor in relation to formulation and pharmacokinetics)

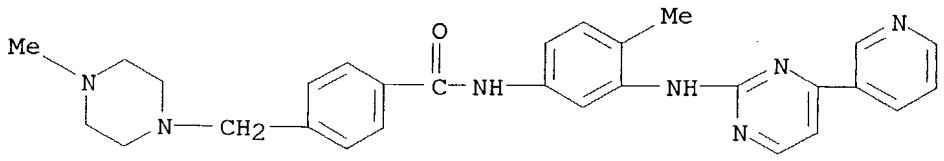
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

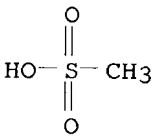
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



=> d his

(FILE 'HOME' ENTERED AT 09:12:52 ON 17 MAY 2004)

FILE 'REGISTRY' ENTERED AT 09:14:23 ON 17 MAY 2004
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 8 SEARCH L1 FULL
L4 1 S 220127-57-1/RN
L5 1 S 152459-95-5/RN
L6 7 S L3 NOT L4
L7 6 S L6 NOT L5

FILE 'CAPLUS' ENTERED AT 09:22:01 ON 17 MAY 2004
L8 10 S RESTINOSIS
L9 446480 S ATHEROSCLEROSIS OR HEART OR CARDIO OR STENT OR ARTEREOSCLEROS
L10 231866 S ARTERIES OR THROMBOSIS OR THROMBOTIC OR PLATELET OR CARDIAC
L11 558207 S L9 OR L10
L12 0 S L3 AND L8
L13 1362 S EMD
L14 577 S L4
L15 182 S L5
L16 4 S L7
L17 106 S L14 AND L11
L18 35 S L15 AND L11
L19 0 S L16 AND L11
L20 6 S L17 AND L18

=> d l17 1-106 fbib ab hitstr

L17 ANSWER 1 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:331787 CAPLUS
TI Treatment of tuberous sclerosis associated neoplasms with **platelet** -derived growth factor receptor tyrosine kinase or bcr-abl tyrosine kinase inhibitors, especially N-phenyl-2-pyrimidineamines

IN Arbiser, Jack
PA USA
SO U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004077661	A1	20040422	US 2003-655407	20030904
			US 2002-408550PP	20020905

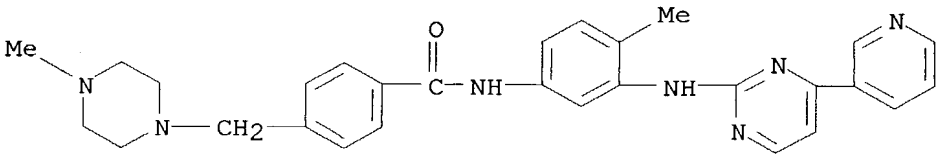
AB The present invention relates to the use of PDGF receptor tyrosine kinase or bcr-abl tyrosine kinase inhibitors, especially of N-phenyl-2-pyrimidine-amine derivs. I (R1 = 4-pyrazinyl, 1-methyl-1H-pyrrolyl, etc.; R2, R3 = H, lower alkyl; R4-8 = nitro, fluoro-substituted lower alkoxy, -N(R9)-C(=X)-(Y)nR10; R9 = H, lower alkyl; X = oxo, thio, imino, N-lower alkylimino, hydroximino, or O-lower alkyl-hydroximino; Y = O, NH; n = 0 or 1; R10 = C5 aliphatic radical, aromatic, etc.) or in pharmaceutically acceptable salt form, in the manufacture of a pharmaceutical composition for the treatment of tuberous sclerosis associated neoplasms; to a method of treatment of warm-blooded animals, including humans, suffering from a tuberous sclerosis associated neoplasms. Cells of SV7tert, a cell line derived from a human angiomyolipoma, were inhibited by 4-(4-methyl-1-piperazin-1-ylmethyl)-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]benzamide.

IT **220127-57-1**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tuberous sclerosis-associated neoplasms treatment with **platelet**-derived growth factor receptor tyrosine kinase or bcr-abl tyrosine kinase inhibitors, especially N-Ph-2-pyrimidineamines)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

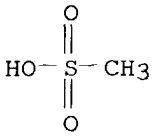
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 2 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:218528 CAPLUS
DN 140:247038
TI Use of specific inhibitors of tyrosine kinases for immunomodulation
IN Zitvogel, Laurence; Auclair, Christian; Tursz, Thomas
PA Institut Gustave Roussy Igr, Fr.
SO Fr. Demande, 50 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2844452	A1	20040319	FR 2002-11545	20020918
	WO 2004026311	A2	20040401	WO 2003-FR2744	20030917

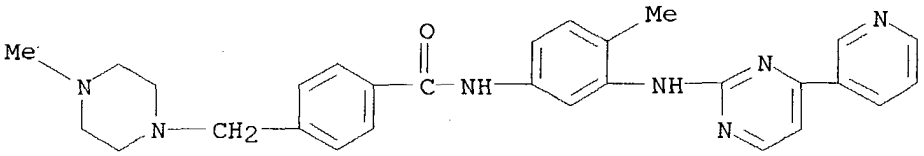
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

FR 2002-11545 A 20020918

AB The invention relates to the use of tyrosine kinase inhibitors for immunomodulation. It more particularly relates to the use of specific tyrosine kinase inhibitors for the preparation of a composition intended for the prevention or the treatment of viral infections, NK cell-sensitive tumors, immunolog. diseases and/or septic shock in a mammal. The inhibitors concerned are more particularly of the inhibitors of tyrosine kinases c-abl (bcr/abl), c-kit and/or of tyrosine kinase associated with the with the PDGF receptor. The tyrosine kinase inhibitors may be used in combination with agents able to potentiate the effect of the inhibitor, such as growth factors Flt3L, GM-CSF and ProGP-4. Thus, tyrosine kinase inhibitor Gleevec stimulated immature dendritic cells to activate NK cells. These inhibitors also inhibited maturation of dendritic cells and thereby limited the inflammatory response.
IT **220127-57-1**, Gleevec
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of specific inhibitors of tyrosine kinases for immunomodulation)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

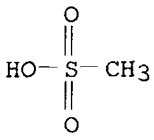
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:207517 CAPLUS
DN 140:245712
TI Molecular targeted treatment. New treatment strategy for patients with chronic myeloid leukemia
AU Usui, Noriko
CS Div. Hematol. Oncol. Dep. Intern. Med., Jikei Univ. Sch. Med., Tokyo, 105-8461, Japan
SO Rinsho Byori (2004), 52(2), 136-144
CODEN: RBYOAI; ISSN: 0047-1860
PB Nippon Rinsho Kensa Igakkai
DT Journal; General Review
LA Japanese
AB A review. Imatinib mesylate is a new drug that can inhibit the tyrosine kinase activity of Bcr-Abl, the receptors for **platelet**-derived growth factor receptor (PDGF) and stem cell factor, or c-kit. Chronic myeloid leukemia (CML) is distinguished by the presence of a reciprocal translocation between chromosomes 9 and 22 that results in a shortened chromosome 22, termed the Philadelphia (Ph) chromosome. As a result of the translocation, a fusion gene called the Bcr-Abl gene is created from two normal cellular genes, encoding a chimeric Bcr-Abl protein with a deregulated tyrosine kinase activity. The expression of Bcr-Abl tyrosine kinase has been shown to be necessary and sufficient for the transformed phenotype of CML cells, Imatinib can block the kinase activity of Bcr-Abl, thus inhibiting the proliferation of Ph-pos. progenitors, and has shown activity against all phases of CML, though responses are most substantial and durable in patients in the chronic phase. An international phase III study which compared the efficacy of imatinib with that of interferon-α combined with low-dose cytarabine in newly diagnosed

chronic-phase CML showed the rate of major cytogenetic response at 24 mo was 90%, including 82% of complete cytogenetic response. These results indicated that imatinib was superior to interferon-containing treatment as a first-line therapy. More than 10,000 patients worldwide, including those in Japan, have been treated with imatinib in clin. trials, and a lot of information has been accumulated on the use of this drug. The aim of this article is to review the use of this drug and the practical management of patients with chronic myeloid leukemia.

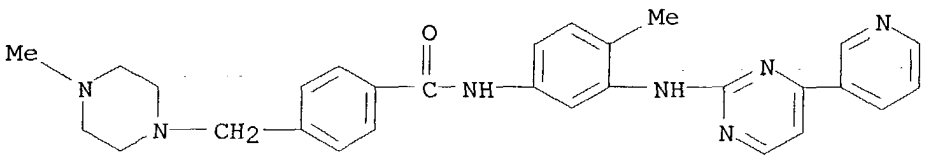
IT **220127-57-1**, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. targeted treatment of chronic myeloid leukemia by imatinib mesylate)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

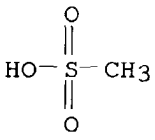
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 4 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:143270 CAPLUS
DN 140:197593
TI PDGFRα oncokinase fusion protein associated with hyperproliferative disease and as imatinib mesylate target in EOL-1 cell
IN Briesewitz, Roger; Griffin, John H.
PA Theravance, Inc., USA
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004015082	A2	20040219	WO 2003-US24992	20030808
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
				US 2002-402330PP	20020809
				US 2003-440491PP	20030116
	US 2004045044	A1	20040304	US 2003-637356	20030808
				US 2002-402330PP	20020809
				US 2003-440491PP	20030116

AB Oncokinase fusion protein associated with hyperproliferative disorders are provided. The fusion polypeptides have a C-terminal tyrosine kinase domain fused to an N-terminal domain that is not normally fused to the C-terminal tyrosine kinase domain and they possess constitutively activated tyrosine kinase activity. The invention provides sequence of protein NM_030917 fused with **platelet**-derived growth factor receptor α from human. The invention also identified deletion of 1 megabase fuses NM_030917 and exon 12 of PDGFRα on human chromosome 4. Also provided are methods of diagnosing disease conditions associated with the fusion polypeptides. In addition, screening assays for identifying agents useful for treating disease conditions associated with such fusion polypeptides and polynucleotides are provided. Furthermore, methods of treating disease conditions associated with the presence of the fusion polypeptides are provided.

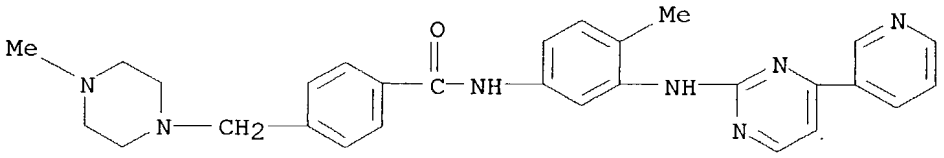
IT **220127-57-1**, Imatinib mesylate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PDGFRα oncokinase fusion protein associated with hyperproliferative disease and as imatinib mesylate target in EOL-1 cell)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

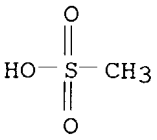
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 5 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:80546 CAPLUS
DN 140:133897
TI Medical devices comprising a protein-tyrosine kinase inhibitor to inhibit restenosis
IN Tremble, Patrice; Carlyle, Wenda
PA Medtronic Ave Inc., USA
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004009147	A1	20040129	WO 2003-US22546	20030717

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-397149PP 20020718

AB Implantable medical devices having an anti-restenotic coatings are disclosed. Specifically, implantable medical devices having coatings of protein-tyrosine kinase inhibitors are disclosed. The anti-restenotic protein-tyrosine kinase inhibitor is imatinib mesylate and its pharmaceutically acceptable derivs. The anti-restenotic medial devices include stents, catheters, microparticles, probes and vascular grafts. The medical devices can be coated using any method known in the art including compounding the protein-tyrosine kinase inhibitor with a biocompatible polymer, e.g., polycaprolactone, prior to applying the coating. Moreover, medical devices composed entirely of biocompatible polymer-protein-tyrosine kinase inhibitor blends are disclosed. Addnl., medical devices having a coating comprising at least one protein-tyrosine kinase inhibitor in combination with at least one addnl. therapeutic agent, such as an antiplatelet agent, antifibrotic agent, proliferation inhibitor, or anti-inflammatory agent, are also disclosed. Furthermore, related methods of using and making the anti-restenotic implantable devices are also disclosed.

IT **220127-57-1**, Imatinib mesylate
RL: DEV (Device component use); PAC (Pharmacological activity); THU

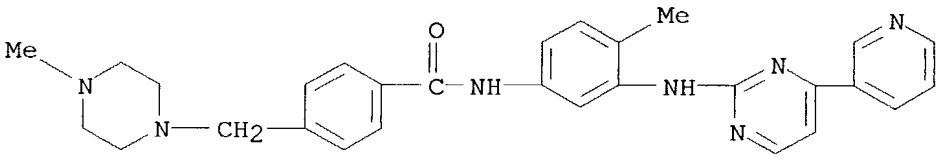
(Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable devices coated with protein-tyrosine kinase inhibitor for drug controlled release and inhibition of restenosis)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

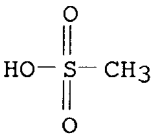
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2004:65410 CAPLUS

DN 140:246405

TI Imatinib mesylate affects the development and function of dendritic cells generated from CD34+ peripheral blood progenitor cells

AU Appel, Silke; Boehmler, Andreas M.; Gruenebach, Frank; Mueller, Martin R.; Rupf, Anette; Weck, Markus M.; Hartmann, Ulrike; Reichardt, Volker L.; Kanz, Lothar; Bruemmendorf, Tim H.; Brossart, Peter

CS Department of Hematology, Oncology, and Immunology, University of Tuebingen, Tuebingen, Germany

SO Blood (2004), 103(2), 538-544
CODEN: BLOOAW; ISSN: 0006-4971

PB American Society of Hematology

DT Journal

LA English

AB Imatinib mesylate (STI571) is a competitive Bcr-Abl tyrosine kinase inhibitor and has yielded encouraging results in treatment of chronic myelogenous leukemia (CML) and gastrointestinal stroma tumors (GISTs). Apart from inhibition of the Abl protein tyrosine kinases, it also shows activity against **platelet**-derived growth factor receptor

(PDGF-R), c-Kit, Abl-related gene (ARG), and their fusion proteins while sparing other kinases. In vitro studies have revealed that imatinib mesylate can inhibit growth of cell lines and primitive malignant progenitor cells in CML expressing Bcr-Abl. However, little is known about the effects of imatinib mesylate on nonmalignant hematopoietic cells. In the current study we demonstrate that in vitro exposure of mobilized human CD34+ progenitors to therapeutic concns. of imatinib mesylate (1-5 μM) inhibits their differentiation into dendritic cells (DCs). DCs obtained after 10 to 16 days of culture in the presence of imatinib mesylate showed concentration-dependent reduced expression levels of CD1a and costimulatory mols. such as CD80 and CD40. Furthermore, exposure to imatinib mesylate inhibited the induction of primary cytotoxic T-lymphocyte (CTL) responses. The inhibitory effects of imatinib mesylate were accompanied by down-regulation of nuclear localized RelB protein. Our results demonstrate that imatinib mesylate can act on normal hematopoietic cells and inhibits the differentiation and function of DCs, which is in part mediated via the nuclear factor κB signal transduction pathway.

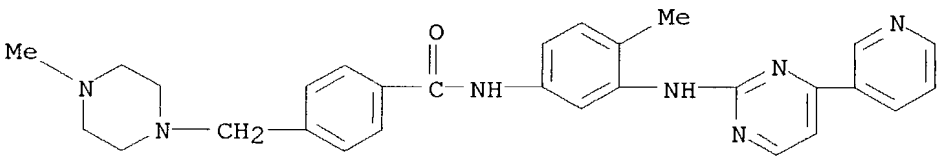
IT **220127-57-1**, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate effect on dendritic cells generated from CD34+ peripheral blood progenitor cells)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

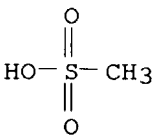
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

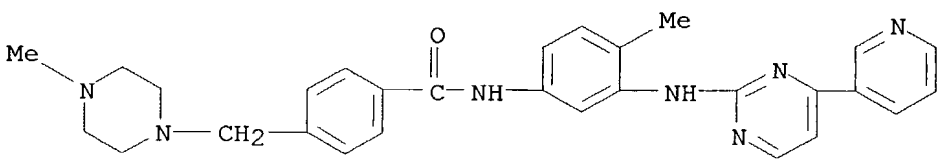


RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:65400 CAPLUS
DN 140:192482
TI Molecular remission and reversal of myelofibrosis in response to imatinib mesylate treatment in patients with the myeloproliferative variant of hypereosinophilic syndrome
AU Klion, Amy D.; Robyn, Jamie; Akin, Cem; Noel, Pierre; Brown, Margaret; Law, Melissa; Metcalfe, Dean D.; Dunbar, Cynthia; Nutman, Thomas B.
CS Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health (NIH), Bethesda, MD, USA
SO Blood (2004), 103(2), 473-478
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB We recently described a subset of patients with a myeloproliferative variant of hypereosinophilic syndrome (MHES) characterized by elevated serum tryptase levels, increased atypical mast cells in the bone marrow, tissue fibrosis, and the presence of the fusion tyrosine kinase, FIP1L1-PDGFRα, which is a therapeutic target of imatinib mesylate. Seven patients with MHES were treated with imatinib mesylate (300-400 mg daily). Clin. improvement and resolution of eosinophilia was observed in all patients, although **cardiac** dysfunction, when present, was not altered by therapy. Reversal of bone marrow pathol., including increased cellularity, the presence of spindle-shaped mast cells, and myelofibrosis, was evident in all patients at 4 to 8 wk following initiation of therapy. This was accompanied by a decrease in activated eosinophils and mast cells in the peripheral blood and bone marrow, resp. Serum tryptase levels declined rapidly to normal levels in all patients and remained in the normal range throughout therapy. Mol. remission, with disappearance of detectable FIP1L1/PDGFRA (F/P) transcripts, was achieved in 5 of 6 patients tested. The lack of reversal of **cardiac** abnormalities and persistence of the F/P mutation in some patients suggests that early intervention with higher doses of imatinib mesylate may be desirable in the treatment of patients with MHES.
IT **220127-57-1**, Imatinib mesylate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. remission and reversal of myelofibrosis in response to imatinib mesylate treatment in patients with myeloproliferative variant of hypereosinophilic syndrome)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

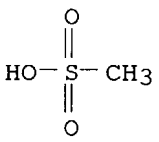
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



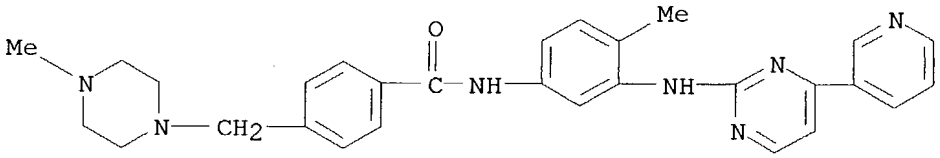
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:65397 CAPLUS
DN 140:87263
TI Clonal evolution and lack of cytogenetic response are adverse prognostic factors for hematologic relapse of chronic phase CML patients treated with imatinib mesylate
AU O'Dwyer, Michael E.; Mauro, Michael J.; Blasdel, Carolyn; Farnsworth, Melanie; Kurilik, Gwen; Hsieh, Yi-Ching; Mori, Motomi; Druker, Brian J.
CS Leukemia Center and Cancer Institute, Oregon Health and Science University, Portland, USA
SO Blood (2004), 103(2), 451-455
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB We followed 141 patients treated with imatinib mesylate (> 300 mg) for chronic phase chronic myelogenous leukemia (CML) following failure of treatment with interferon. During 12 mo from the start of imatinib mesylate treatment, 96.5% achieved a complete hematol. response, 47.0% achieved a major cytogenetic response, and 32.4% achieved a complete cytogenetic response. The proportion of patients with hematol. relapse was 10.9% at 12 mo and 14.6% at 18 mo. In a univariate Cox regression anal., the only pretreatment characteristics that correlated with an increased risk of hematol. relapse were Hb level less than 120 g/L (12 g/dL) (P = .02), increased bands in the peripheral blood (P = .01), and clonal evolution (P < .0001). In a multivariate anal., an elevated **platelet** count (P = .03) and clonal evolution (P < .0001) were the only significant factors for hematol. relapse. During treatment, the absence of a major cytogenetic response within the first 6 mo also significantly correlated with relapse (P = .03). Notably, patients failing to achieve a major cytogenetic response by 6 mo had a significantly higher rate of hematol. relapse (27%) compared with those who achieved a major cytogenetic response by 6 mo (3%), and patients with clonal evolution had a significantly higher risk of hematol. relapse (50%) than those without clonal evolution (9%).
IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate for chronic myelogenous leukemia and prognostic factors for relapse)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-

pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

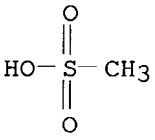
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:47375 CAPLUS
DN 140:104713
TI The significance of myelosuppression during therapy with imatinib mesylate in patients with chronic myelogenous leukemia in chronic phase
AU Sneed, Thomas B.; Kantarjian, Hagop M.; Talpaz, Moshe; O'Brien, Susan; Rios, Mary Beth; Bekele, B. Nebiyou; Zhou, Xian; Resta, Debra; Wierda, William; Faderi, Stefan; Giles, Francis; Cortes, Jorge E.
CS Department of Leukemia, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA
SO Cancer (New York, NY, United States) (2004), 100(1), 116-121
CODEN: CANCAR; ISSN: 0008-543X
PB John Wiley & Sons, Inc.
DT Journal
LA English
AB Imatinib mesylate induces high rates of hematol. and cytogenetic response in patients with chronic myelogenous leukemia (CML). During therapy with imatinib, up to 45% of patients with CML reportedly experience myelosuppression ≥ Grade 3, requiring interruption of therapy and/or dose redns. The significance of myelosuppression for response to imatinib is unknown. The authors analyzed 143 patients with late chronic-phase CML who were treated with imatinib after failing interferon. Univariate and multivariate analyses were performed to determine patient characteristics that were correlated with myelosuppression response and the association between myelosuppression and cytogenetic response.

Neutropenia ≥ Grade 3 (according to National Cancer Institute Common Toxicity Criteria) occurred in 64 patients (45%), and thrombocytopenia ≥ Grade 3 occurred in 31 patients (22%). Any myelosuppression ≥ Grade 3 was associated with a lower rate of major (P = 0.04) or complete (P = 0.01) cytogenetic responses. This was more pronounced with myelosuppression that lasted > 2 wk. The major cytogenetic response rate was 58% with Grade ≥ 3 myelosuppression compared with a rate of 75% without Grade ≥3 myelosuppression (P = 0.03); the complete cytogenetic response rates were 36% and 63%, resp. (P = 0.001). In a multivariate anal., pretreatment **platelet** count, imatinib dose redns., and duration of myelosuppression were associated significantly with response. Myelosuppression is an independent adverse factor for achieving cytogenetic response with imatinib in patients with CML. Intervention with hematopoietic growth factors in patients with CML who are treated with imatinib should be investigated.

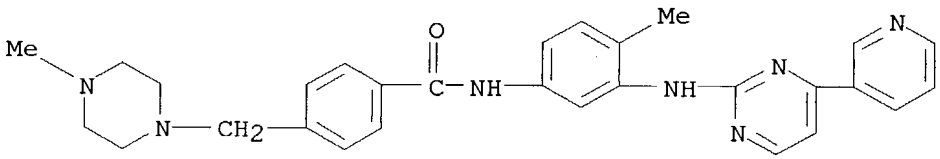
IT **220127-57-1,** Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate-associated myelosuppression in patients with chronic myelogenous leukemia)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

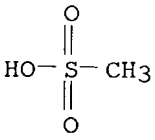
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:32056 CAPLUS
DN 140:87256

TI Imatinib mesylate therapy of chronic phase chronic myeloid leukemia resistant or intolerant to interferon: results and prognostic factors for response and progression-free survival in 150 patients

AU Cervantes, Francisco; Hernandez-Boluda, Juan-Carlos; Steegmann, Juan-Luis; Conde, Eulogio; Alvarez-Larran, Alberto; Lopez-Jimenez, Javier; Osorio, Santiago; Villalon, Lucia; Camos, Mireia; Garcia-Conde, Javier; Odriozola, Jesus

CS Hematology Departments, Hospital Clinic, IDIBAPS, Barcelona, Spain

SO Haematologica (2003), 88(10), 1117-1122
CODEN: HAEMAX; ISSN: 0390-6078

PB Ferrata Storti Foundation

DT Journal

LA English

AB Background and Objectives: Imatinib mesylate has recently been shown to be highly effective in chronic-phase chronic myeloid leukemia (CML). The results of imatinib treatment in chronic-phase CML patients resistant or intolerant to interferon (IFN) and the factors predicting therapeutic response and progression-free survival were analyzed. Design and Methods: One hundred and fifty patients with chronic-phase CML resistant (n = 111) or intolerant (n = 39) to IFN were treated with imatinib. Prognostic factors for response and disease progression were assessed by multivariate anal. Results: The median time from diagnosis was 43 mo (0.5 - 188), median IFN therapy 21.5 mo (0.5 - 140) and median follow-up from starting imatinib 13.6 mo (range: 3 - 23). Complete hematol. response was achieved in 96 of 97 patients. Complete, partial and minor cytogenetic responses were present in 44%, 22%, and 8% of patients at 12 mo. Grade III-IV neutropenia, thrombocytopenia, and anemia developed in 33%, 16%, and 6% of patients, resp. Sixty-five patients discontinued treatment for a median of 4 wk (1-36) due to toxicity. The rate of progression-free survival (lack of accelerated/blastic phase with persistent response) was 89.2% (95% CI: 84-94.4) at 12 mo and 80.2% (95% CI: 72.2 - 88.2) at 18 mo. Platelets > 450 + 109/L and treatment discontinuation > 4 wk were associated with a lower rate of major (complete plus partial) cytogenetic response. Patients in Sokal's high-risk group and those who did not achieve a major cytogenetic response had significantly shorter progression-free survival. Interpretation and Conclusions: Imatinib is highly effective in chronic-phase CML patients resistant or intolerant to IFN, especially in those with normal **platelet** counts and in those not requiring prolonged treatment discontinuation due to neutropenia.

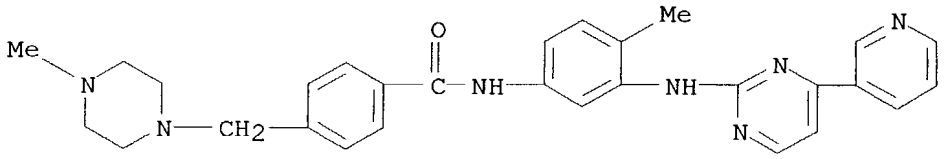
IT **220127-57-1**, Glivec
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate (Glivec) therapy for patients with chronic-phase chronic myeloid leukemia resistant or intolerant to interferon)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

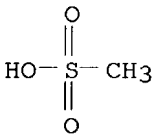
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:20448 CAPLUS
DN 140:87676
TI Derivatives of gambogic acid and analogs as activators of caspases and inducers of apoptosis
IN Tseng, Ben; Sirisoma, Nilantha Sudath; Cai, Sui Xiong; Zhang, Han-Zhong; Kasibhatla, Shailaja; Ollis, Kristin P.; Drewe, John A.
PA Cytovia, Inc., USA
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004002428	A2	20040108	WO 2003-US20668	20030701
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			US 2002-392358PP	20020701
			US 2002-413649PP	20020926
US 2004082066	A1	20040429	US 2003-609670	20030701
			US 2002-392358PP	20020701
			US 2002-413649PP	20020926

OS MARPAT 140:87676
AB The invention is directed to derivs. of gambogic acid and analogs thereof.

Exemplary gambogic acid derivs. of the present invention include, among others, derivs. substituted in the C10 and C28 positions of gambogic acid. The present invention also relates to the discovery that certain preferred compds. of the invention are activators of caspases and inducers of apoptosis. Therefore, the activators of caspases and inducers of apoptosis of this invention can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs.

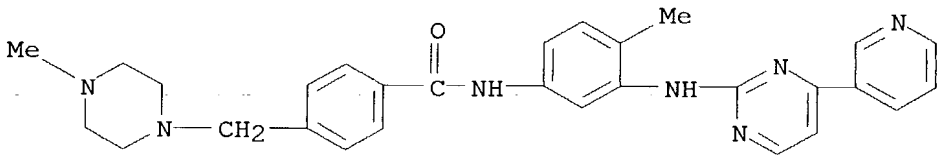
IT **220127-57-1**, Gleevec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivs. of gambogic acid and analogs as activators of caspases and inducers of apoptosis)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

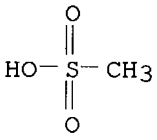
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

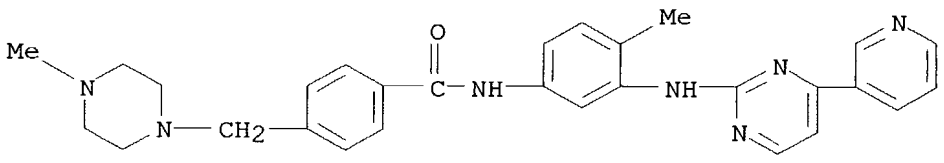


L17 ANSWER 12 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:13218 CAPLUS
DN 140:70552
TI Imatinib mesylate in idiopathic and postpolycythemic myelofibrosis
AU Hasselbalch, Hans Carl; Bjerrum, Ole Weiss; Jensen, Bjarne Anker; Clausen, Nielsaage Toffner; Hansen, Per Boye; Birgens, Henrik; Therkildsen, Marianne Hamilton; Ralfkiaer, Elisabeth
CS Department of Medicine, Division of Hematology and Oncology, Roskilde Hospital, Roskilde, 4000, Den.
SO American Journal of Hematology (2003), 74(4), 238-242
CODEN: AJHEDD; ISSN: 0361-8609
PB Wiley-Liss, Inc.

DT Journal
LA English
AB Imatinib mesylate targets the ATP-binding sites of the protein tyrosine kinase domains associated with Bcr-abl, the **platelet**-derived growth factor (PDGF) and c-kit. In idiopathic myelofibrosis (IMF) PDGF is considered to be one of the growth factors responsible for the development of bone marrow fibrosis. Recently, it has been shown that imatinib has antifibrogenic effect on bone marrow fibrosis in chronic myelogenous leukemia. Treatment with imatinib alone in IMF has been associated with significant side effects. In this study, the safety and efficacy of imatinib therapy in IMF, either administered as a single agent or in combination with hydroxyurea (HU) and/or alpha-interferon (IFN-α) are evaluated. Eleven patients (median age, 63 yr; range, 33-82 yr) with IMF (n = 8) or postpolycythemic myelofibrosis (PPMF) (n = 3) were studied. All patients had been treated with HU (n = 9) and/or IFN (n = 7) before study entry. In all but one patient, treatment with these agents was discontinued when imatinib therapy was instituted. One patient continued IFN when treatment with imatinib was started. Imatinib was given at a dose of 400 mg/day. Nine patients were in an advanced disease phase. The patients have been followed for a median period of 2 mo (range, 0.5-12 mo). Treatment with imatinib has been stopped in six patients (55%), because of overt side effects (n = 4), recurrence of transitory dizziness and visual defects owing to a rising **platelet** count (n = 1), or the occurrence of an acute subdural hemorrhage that was evacuated without neurol. deficits (n = 1). In nine patients imatinib treatment was followed by a rise in leukocyte and **platelet** counts that required combination with HU or IFN. The combined treatment modalities were followed by a rapid decrease in cell counts and were well tolerated apart from IFN side effects. A beneficial effect of imatinib was documented in three patients. It is concluded that leukocytosis and thrombocytosis are seen in most patients with myelofibrosis during treatment with imatinib. Combination therapy with HU or IFN seems safe and well tolerated and followed by a decrease in disease activity. A subgroup of patients in an early disease phase might benefit from imatinib therapy alone.
IT **220127-57-1**, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate in idiopathic and postpolycythemic myelofibrosis)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

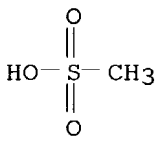
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 13 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:931221 CAPLUS
DN 140:789
TI Modulators of c-Abl activation for control of glycosaminoglycan chain length in a cell, and therapeutic use
IN Little, Peter James
PA Baker Medical Research Institute, Australia
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003097110	A1	20031127	WO 2003-AU608	20030520

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002-2430 A 20020520

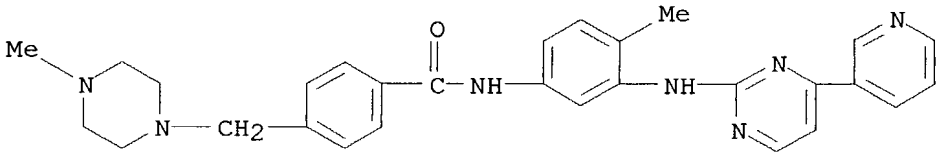
AB The invention relates to the finding of a novel therapeutic target which is implicated in regulating glycosaminoglycan (GAG) length, and the use of this target particularly for regulating lipoprotein binding. More particularly, the invention relates to the use of this target for methods of treating and preventing conditions associated with lipoprotein binding in tissues or blood vessels. More specifically, the invention resides in the use of the new target as a key biochem. target for the prevention and treatment of **atherosclerosis** and identifies useful therapeutic agents which may act on the target. Accordingly, in a first aspect of the invention, a method is provided for controlling GAG chain length in a cell, the method comprising modifying activation of c-Abl in the cell. A c-Abl inhibitor according to the invention is imatinib.

IT **220127-57-1**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-Abl activation modulators for control of glycosaminoglycan chain

length in cell, and therapeutic use)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

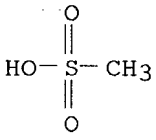
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 14 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:917644 CAPLUS
DN 140:123151
TI SB-431542 and Gleevec inhibit transforming growth factor-β-induced proliferation of human osteosarcoma cells
AU Matsuyama, Shigeo; Iwadate, Manabu; Kondo, Miki; Saitoh, Masao; Hanyu, Aki; Shimizu, Kiyoshi; Aburatani, Hiroyuki; Mishima, Hiromu K.; Imamura, Takeshi; Miyazono, Kohei; Miyazawa, Keiji
CS Department of Molecular Phathology, Graudate School of Medicine, University of Tokyo, Tokyo, Japan
SO Cancer Research (2003), 63(22), 7791-7798
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Transforming growth factor-β (TGF-β) has growth-stimulating effects on mesenchymal cells and several tumor cell lines. The signaling pathway for this effect is, however, not well understood. The authors examined how TGF-β stimulates proliferation of MG63 human osteosarcoma cells. Two distinct type I receptors for TGF-β, ALK-1 and ALK-5, were expressed and functional in MG63 cells. Of these two receptors, ALK-5 appears to be responsible for the growth stimulation because

expression of constitutively active ALK-5, but not ALK-1, stimulated proliferation of MG63 cells. SB-431542 (0.3 μM), a novel inhibitor of ALK4/5/7 kinase, suppressed TGF-β-induced growth stimulation. DNA microarray anal. as well as quant. real-time PCR anal. of RNAs from TGF-β-treated cells demonstrated that several growth factors, including **platelet**-derived growth factor AA, were induced in response to TGF-β in MG63 cells. Gleevec (1 μM) as well as AG1296 (5 μM) inhibited TGF-β-induced growth stimulation of MG63 cells, suggesting that **platelet**-derived growth factor AA was mainly responsible for the growth-stimulatory effect of TGF-β. The authors also examined the mechanisms of perturbation of growth-suppressing signaling in MG63 cells. The authors found that expression of c-Myc, which is down-regulated by TGF-β in many other cells, was up-regulated in MG63 cells, suggesting that up-regulation of c-Myc expression may be the mechanism canceling growth-suppressing signaling of TGF-β in MG63 cells.

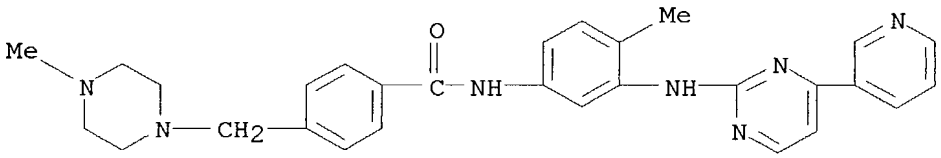
IT **220127-57-1**, Gleevec
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SB-431542 and Gleevec inhibit transforming growth factor-β-induced proliferation of human osteosarcoma cells in relation to induction of growth factors and control of cell-cycle regulators by TGF-β)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

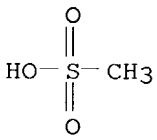
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 15 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:912990 CAPLUS
DN 139:375014
TI Methods and compositions with N-phenyl-2-pyrimidine compounds inhibiting **platelet** derived growth factor receptor for the treatment of graft failure
IN Sukhatme, Vikas P.
PA Beth Israel Deaconess Medical Center, USA
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003094904	A1	20031120	WO 2003-US14916	20030513

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-380180PP 20020513
US 2003-464023PP 20030418

OS MARPAT 139:375014
AB The present invention provides methods and compns. for treating graft failure resulting from neointimal hyperplasia. These methods and compns. feature the use of **platelet** derived growth factor receptor (PDGFR) inhibitor compds., such as N-phenyl-2-pyrimidine compds. (e.g., imatinib mesylate) to inhibit the biol. activity of the PDGFR and treat AV graft failure. Gleevec and rapamycin inhibited smooth muscle cell migration.
IT **220127-57-1**, Imatinib mesylate
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-Ph-2-pyrimidine compds. inhibiting **platelet** derived growth factor receptor for treatment of graft failure)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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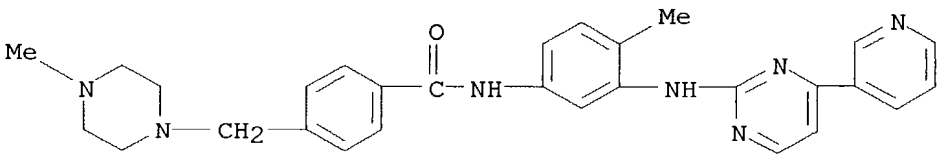
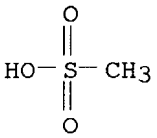


CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 16 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:892941 CAPLUS
DN 139:347736
TI Method of using optical interrogation to determine a biological property of a cell or population of cells
IN Schnabel, Catherine A.; Diver, Jonathan; Kariv, Ilona; Forster, Anita; Mercer, Elinore; Hall, Jeffrey; Nova, Tina; Soohoo, William; Kohrumel, Josh; Nguyen, Phan; Zhang, Haichuan; Tu, Eugene; Chung, Thomas D. Y.; Lykstad, Kristie Lynn; Wang, Mark M.; Butler, William Frank; Raymond, Daniel E.
PA Genoptix, Inc., USA
SO PCT Int. Appl., 245 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 20

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003093496	A1	20031113	WO 2003-US13735	20030430
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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			US 2002-399931PP	20020730
			US 2002-400936PP	20020801
			US 2002-243611 A	20020912
			US 2002-324926 A	20021219
			US 2003-427748 A	20030429
US 2003124516	A1	20030703	US 2002-243611	20020912
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PATENT FAMILY INFORMATION:

FAN 2002:368758

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PI	WO 2002039104	A1	20020516	WO 2001-US47421	20011109
	WO 2002039104	B1	20020801		

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FAN 2002:610486

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	US 2003007894	A1	20030109	US 2001-845245 20010427

FAN 2002:674682

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PI	US 2002123112	A1	20020905	US 2001-993375 20011114 US 2000-248451PP 20001113 US 2001-843902 A 20010427 US 2001-845245 A220010427
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FAN 2002:716953

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PI	US 2002132315	A1	20020919	US 2001-993326 20011114 US 2000-248451PP 20001113 US 2001-845245 A220010427
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	WO 2003062867	A2	20030731	WO 2003-US340 20030106
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-53507 A 20020117

FAN 2003:21842

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FAN 2004:34161

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FAN 2004:142690

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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US 2003-427748 A 20030429

FAN 2004:219917

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			US 2001-993377	A220011114
			US 2002-53507	A220020117

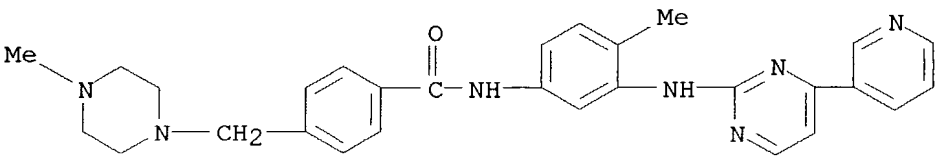
AB Optophoretic methods are used to determine one or more biol. properties or changes in biol. properties of one or more cells or cellular components. The methods use optical or photonic forces to select, identify, characterize, and/or sort whole cells or groups of cells. The methods are useful in a number of applications, including, but not limited to, drug screening applications, toxicity applications, protein expression applications, rapid clonal selection applications, biopharmaceutical monitoring and quality control applications, cell enrichment applications, viral detection, bacterial drug sensitivity screening, environmental testing, agricultural testing, food safety testing, personalized medicine applications as well as biohazard detection and anal.

IT **220127-57-1**, Gleevec
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cells response to; apparatus and method for optical interrogation to determine
biol. properties of cells or population of cells)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

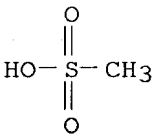
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 17 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:877647 CAPLUS
DN 140:108
TI New drug targeting treatment - Glivec
AU Sun, Xue-mei; Brady, Ben
CS Nanjing Drum Tower Hospital, Nanjing University Medical College, Nanjing, 210008, Peop. Rep. China
SO Chinese Journal of Cancer Research (2003), 15(3), 235-239
CODEN: CJCRFH; ISSN: 1000-9604
PB Chinese Journal of Cancer Research
DT Journal; General Review
LA English
AB A review. This review evaluates the role of Glivec in the treatment of chronic myelogenous leukemia and other malignant tumors. Preclin. and clin. evidence showed that Glivec demonstrated a potent and specific inhibition on BCR-ABL pos. leukemias and other malignant tumors in which overexpression of c-kit and PDGFR-β played a major role in their pathogenesis. Glivec has induced complete hematol. responses in up to 98% of patients evaluated in clin. trials. It is a very successful drug that supported the idea of targeted therapy through inhibition of tyrosine kinases. Although it is still in the early stages of clin. development and the resistance to Glivec remains to be a problem needed further study, a great deal has been learned from these research and observation. And

with the increasing data, mol. targeting therapy will play much more important role in the treatment of malignant tumors. With the better understanding of the pathogenesis of malignant tumors, well-designed drugs targeting the specific mol. abnormalities with higher efficacy and lower side effect will benefit numerous patients with malignant tumors.

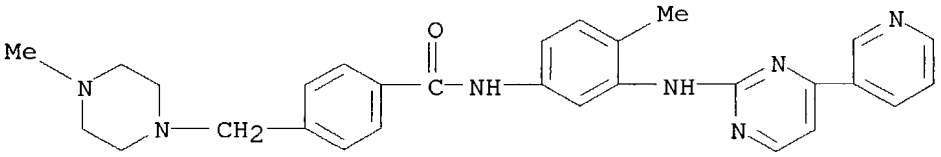
IT **220127-57-1**, Glivec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new drug targeting treatment - Glivec for treatment of chronic myelogenous leukemia and other malignant tumors)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

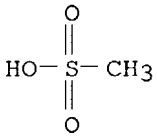
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 18 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:875113 CAPLUS
DN 139:345924
TI PDGF receptor tyrosine kinase inhibitors for the treatment of polycythemia vera
IN Kantarjian, Hagop
PA Board of Regents, the University of Texas System, USA
SO PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 2003090750	A1	20031106	WO 2003-IB1632	20030422

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

US 2002-375143PP 20020424

AB The invention discloses the treatment of polycythemia vera by administration of N-[5-(4-(4-methylpiperazinomethyl)benzoylamido)-2-methylphenyl]-4-(3-pyridyl)-2-pyrimidineamine or 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-((4-(3-pyridinyl)-2-pyrimidinyl)amino)phenyl]benzamide in free form or in pharmaceutically acceptable salt form.

IT **220127-57-1**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

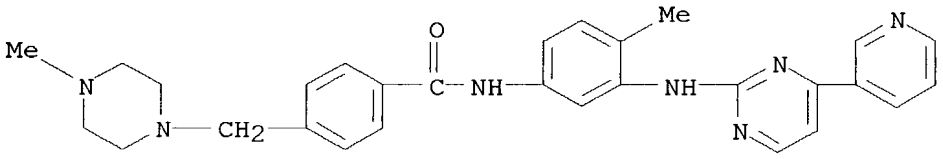
(PDGF receptor tyrosine kinase inhibitors for treatment of polycythemia vera)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

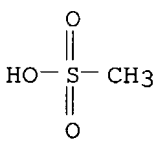
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



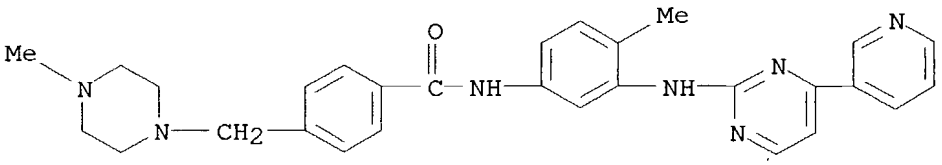
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 19 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:873774 CAPLUS
DN 139:345519
TI CHIC2 deletion, a surrogate for FIP1L1-PDGFRA fusion, occurs in systemic mastocytosis associated with eosinophilia and predicts response to imatinib mesylate therapy
AU Pardanani, Animesh; Ketterling, Rhett P.; Brockman, Stephanie R.; Flynn, Heather C.; Paternoster, Sarah F.; Shearer, Brandon M.; Reeder, Terra L.; Li, Chin-yang; Cross, Nicholas C. P.; Cools, Jan; Gilliland, D. Gary; Dewald, Gordon W.; Tefferi, Ayalew
CS Divisions of Hematology and Internal Medicine, Laboratory Genetics, and Hematopathology, Mayo Clinic, Rochester, MN, USA
SO Blood (2003), 102(9), 3093-3096
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Imatinib mesylate is effective in the treatment of hematol. malignancies that are characterized by either abl- or PDGFRβ-activating mutations. The drug is also active in a subset of patients with eosinophilic disorders and systemic mast cell disease (SMCD). Recently, a novel tyrosine kinase that is generated from fusion of the Fip1-like 1 (FIP1L1) and PDGFRα (PDGFRA) genes has been identified as a therapeutic target for imatinib mesylate in hypereosinophilic syndrome (HES). We used fluorescence in situ hybridization (FISH) to detect deletion of the CHIC2 locus at 4q12 as a surrogate for the FIP1L1-PDGFRA fusion. CHIC2 deletion was observed in bone marrow cells for 3 of 5 patients with SMCD associated with eosinophilia. Deletion of this locus and expression of the FIP1L1-**platelet**-derived growth factor receptor α (PDGFRA) fusion was also documented in enriched eosinophils, neutrophils, or mononuclear cells by both FISH and reverse transcriptase-polymerase chain reaction (RT-PCR) for one patient. While all 3 patients with the FIP1L1-PDGFRA rearrangement achieved a sustained complete response with imatinib mesylate therapy, the other two, both carrying the c-kit Asp816 to Val (Asp816Val) mutation, did not. These observations suggest that the FIP1L1-PDGFRA rearrangement occurs in an early hematopoietic progenitor and suggests that the mol. pathogenesis for a subset of SMCD patients is similar to that of HES. Screening for the FIP1L1-PDGFRA rearrangement and Asp816Val mutation will advance rational therapy decisions in SMCD.
IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CHIC2 deletion, a surrogate for FIP1L1-PDGFRA fusion, occurs in systemic mastocytosis associated with eosinophilia and predicts response to imatinib mesylate therapy)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

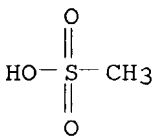
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 20 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:847713 CAPLUS
DN 140:209936
TI STI571 enhances the therapeutic index of epothilone B by a tumor-selective increase of drug uptake
AU Pietras, Kristian; Stumm, Michael; Hubert, Martine; Buchdunger, Elisabeth; Rubin, Kristofer; Heldin, Carl-Henrik; McSheehy, Paul; Wartmann, Markus; Oestman, Arne
CS Ludwig Institute for Cancer Research, Uppsala, SE-751 24, Swed.
SO Clinical Cancer Research (2003), 9(10, Pt. 1), 3779-3787
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB Purpose: The purpose is to investigate whether STI 571, through **platelet**-derived growth factor receptor inhibition, enhances the therapeutic response to the chemotherapeutic drug epothilone B (EPO 906) and, if so, to analyze the mechanisms underlying the effect. Exptl. Design: SCID mice with s.c. human anaplastic thyroid carcinomas were treated with different doses of EPO 906 alone or in combination with STI 571 and with different timing of STI 571 and EPO 906 administration. Tumor growth, tumor interstitial fluid pressure (IFP), and uptake of EPO 906 in tumors and normal organs were monitored. Results: STI 571 potentiated the therapeutic effect of EPO 906. Tumors subjected to combination treatment were >40% smaller than those subjected to monotreatment with EPO 906. The improved efficacy was matched by reduced tumor IFP and a 3-fold increase in the tumor levels of EPO 906. No significant increase of EPO 906 levels was seen in liver, kidney, or the intestinal tract. Cotreatment did not reduce the tolerability of EPO 906, as determined by measuring body weight throughout treatment. STI 571-induced reduction in tumor IFP and increase in tumor uptake required a min. of three daily doses of STI 571 and was not observed 3 days after last treatment with STI 571. The enhancement of EPO 906 therapeutic efficacy was only observed when STI 571 was scheduled in a manner associated with reduced tumor IFP and

increased tumor uptake of EPO 906. Conclusions: We conclude that STI 571 increases the therapeutic index of EPO 906 by selectively increasing the EPO 906 uptake in tumors. The correlations between STI 571 effects on tumor IFP and tumor drug uptake of EPO 906 suggest a causal relationship between these phenomena. The study thus validates STI 571 for combination treatment to enhance the therapeutic index of EPO 906 in particular and, possibly, of chemotherapeutics in general.

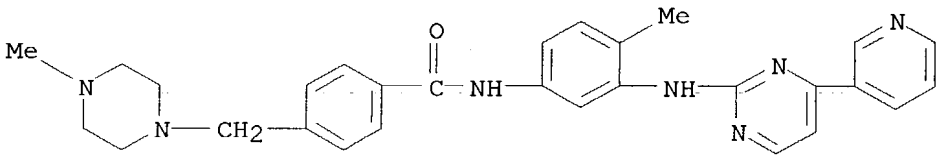
IT **220127-57-1**, STI 571
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571 enhancement of epothilone B therapeutic index by tumor-selective increase of drug uptake in SCID mice with s.c. human anaplastic thyroid carcinomas)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

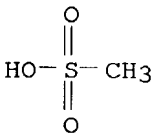
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 21 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:836920 CAPLUS
DN 139:328378
TI Drug eluting vascular **stent** and method of treating hyperproliferative vascular disease
IN Moussa, Issam
PA USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086497	A1	20031023	WO 2003-IB1230	20030404

PI WO 2003086497 A1 20031023 WO 2003-IB1230 20030404
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002-373107PP 20020416

AB This invention provides a drug eluting vascular **stent** and a method of preventing or treating hyperproliferative vascular disease in a mammal by administering an antiproliferative effective amount of imatinib mesylate, alone or in combination with other compds., via a vascular **stent**. The hyperproliferative vascular disease may be caused by vascular injury, percutaneous transluminal coronary angioplasty,etc.

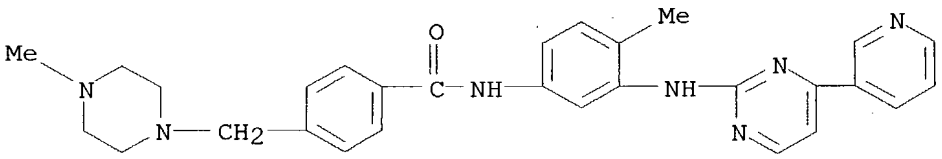
IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug eluting vascular **stent** and method of treating hyperproliferative vascular disease)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

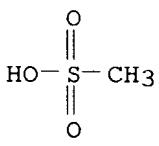
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 22 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:836581 CAPLUS
DN 139:345919
TI Regeneration of endogenous myocardial tissue by induction of neovascularization
IN Itescu, Silviu
PA USA
SO U.S. Pat. Appl. Publ., 51 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003199464	A1	20031023	US 2002-128738	20020423
WO 2003090512	A2	20031106	WO 2003-US12768	20030423

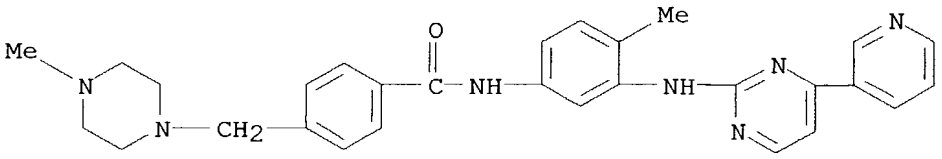
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-128738 A220020423

AB This invention provides a method of treating a disorder of a subject's **heart** involving loss of cardiomyocytes which comprises administering to the subject an amount of an agent effective to cause cardiomyocyte proliferation within the subject's **heart** to thereby treat the disorder. This invention further provides the instant method wherein the agent is human endothelial progenitor cells. This invention also provides methods of determining the susceptibility of a cardiomyocyte in a subject to apoptosis.
IT **220127-57-1**, STI-571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(regeneration of endogenous myocardial tissue by induction of neovascularization using human endothelial progenitor cells and inhibitor of c-Abl tyrosine kinase activation)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

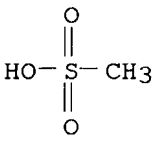
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

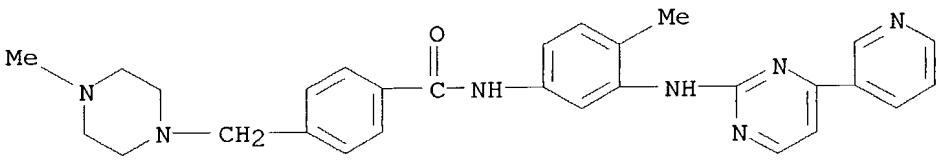


L17 ANSWER 23 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:835292 CAPLUS
DN 139:359229
TI Granulocyte colony-stimulating factor reverses cytopenia and may permit cytogenetic responses in patients with chronic myeloid leukemia treated with imatinib mesylate
AU Marin, David; Marktel, Sarah; Foot, Nicola; Bua, Marco; Olavarria, Eduardo; Goldman, John M.; Apperley, Jane F.
CS Department of Hematology, Imperial College at Hammersmith Hospital, London, W12 0NN, UK
SO Haematologica (2003), 88(2), 227-229
CODEN: HAEMAX; ISSN: 0390-6078
PB Ferrata Storti Foundation
DT Journal
LA English
AB Imatinib mesylate induces major or complete cytogenetic responses in the majority of patients with chronic myeloid leukemia (CML) in chronic phase. However, 15-40% of patients develop neutropenia and/or thrombocytopenia that makes it necessary to reduce the dosage or to interrupt treatment. Patients with recurrent cytopenias may be less likely to obtain cytogenetic responses. We speculated that low doses of granulocyte colony-stimulating factor (G-CSF) in conjunction with imatinib might offer clin. benefit. Eleven patients with CML in chronic (n = 9) or accelerated (n = 2) phase who could not tolerate 300 mg/day and had no cytogenetic response after 6 mo of imatinib treatment received G-CSF in combination with imatinib. Ten of the 11 patients could then tolerate doses of imatinib equal to or greater than 300 mg/day and 7 patients achieved major (n = 6) or complete (n = 1) cytogenetic responses. We conclude that G-CSF reverses the hematol. toxicity of imatinib and may thereby increase the proportion of cytogenetic responses.
IT **220127-57-1**, Glivec
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(granulocyte colony-stimulating factor reverses cytopenia and may permit cytogenetic responses in patients with chronic myeloid leukemia treated with imatinib mesylate)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

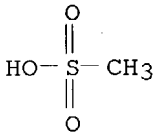
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 24 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:825330 CAPLUS
DN 139:345183
TI Targeting PDGF receptors in cancer - rationales and proof of concept clinical trials
AU George, Daniel
CS Dana-Farber Cancer Institute, Boston, MA, USA
SO Advances in Experimental Medicine and Biology (2003), 532(New Trends in Cancer for the 21st Century), 141-151
CODEN: AEMBAP; ISSN: 0065-2598
PB Kluwer Academic/Plenum Publishers
DT Journal; General Review
LA English
AB A review. The **platelet**-derived growth factors (PDGF) are a pleotrophic family of peptide growth factors that signal through cell surface, tyrosine kinase receptors (PDGFR) and stimulate various cellular functions including growth, proliferation, and differentiation. To date, PDGF expression has been demonstrated in a number of different solid tumors, from glioblastomas to prostate carcinomas. In these various tumor types, the biol. role of PDGF signaling can vary from autocrine stimulation of cancer cell growth to subtler paracrine interactions involving adjacent stroma and vasculature. The tyrosine kinase inhibitor imatinib mesylate (formerly ST1571, Gleevec, Novartis Pharmaceuticals Corp, East Hanover,

NJ) blocks activity of the Bcr-Abl oncoprotein and the cell surface tyrosine kinase receptor c-Kit, and as such was recently approved for several indications in the treatment on chronic myeloid leukemia and gastrointestinal stromal tumors. In both of these examples the target protein was identified by an oncogenic, activating mutation. Imatinib mesylate is also a potent inhibitor of PDGFR kinase and is currently being evaluated for the treatment of chronic myelomonocytic leukemia and glioblastoma multiforme, based upon evidence in these diseases of activating mutations in PDGFR. However, the PDGF pathway may represent a therapeutic target in other solid tumors in which it is not part of the oncogenic transformation. In order to investigate the potential biol. implications of inhibiting PDGFR in these tumor types, clin. trials that investigate both established clin. endpoints of response and benefit, as well as surrogate endpoints that describe the biol. significance of PDGF inhibition in vivo are needed.

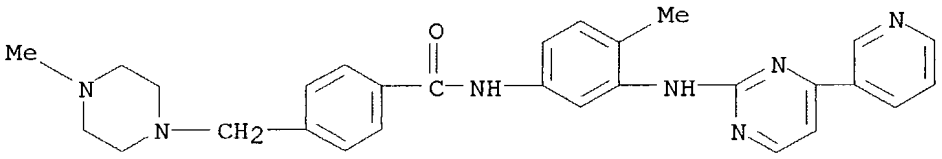
IT **220127-57-1**, Gleevec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PDGF receptors inhibitors for treatment of cancer)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

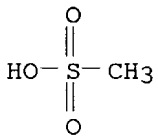
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 25 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:792914 CAPLUS
DN 140:192389
TI Imatinib mesylate (STI571; Glivec)-a new approach in the treatment of

biliary tract cancer?

AU Wiedmann, Marcus; Kreth, Florian; Feisthammel, Juergen; Deininger, Michael; Moessner, Joachim; Caca, Karel

CS Department of Internal Medicine II, University of Leipzig, Leipzig, Germany

SO Anti-Cancer Drugs (2003), 14(9), 751-760
CODEN: ANTDEV; ISSN: 0959-4973

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB Non-resectable biliary tract cancer is associated with poor prognosis due to widespread resistance to chemotherapeutic agents and radiotherapy. It is therefore essential to explore new therapeutic approaches like the inhibition of tyrosine kinases. The aim of this study was to determine the expression of c-kit and **platelet**-derived growth factor (PDGF) receptors (PDGFRs) and the effects of the tyrosine kinase inhibitor imatinib±5-fluorouracil (5-FU) on proliferation and apoptosis in biliary tract cancer cell lines. The expression of c-kit and PDGFR mRNA was examined in 12 biliary tract cancer cell lines using RT-PCR. Cells were treated with imatinib (1, 10, 20 and 50 μmol/l)±5-FU (0.1 μg/mL) for 6 days and inhibition of cell growth was assessed by manual cell counting. Cell proliferation and apoptosis were analyzed by flow cytometry of BrdU and Annexin-V/propidium iodide-stained cells. c-kit and PDGF mRNA expression was detected in 50 and 75%, resp. Imatinib (10 and 20 μmol/l) alone inhibited cell growth significantly higher in c-kit+ cell lines ($p<0.02$) and inhibition was independent of PDGFR status. The combination with 5-FU increased the effect of imatinib mesylate in all cell lines. Treatment of cells with imatinib±5-FU was associated with a significant induction of apoptosis, but no inhibition of proliferation. We conclude that imatinib alone exerts marked effects on c-kit+ biliary tract cancer cell lines only at intermediate and high concns., but there is a potential role of low-dose imatinib in combination with 5-FU for the treatment of biliary tract cancers.

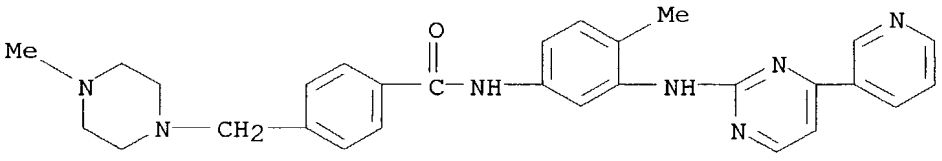
IT **220127-57-1**, Imatinib mesylate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(expression of c-kit and PDGF receptors and effects of tyrosine kinase inhibitor imatinib and 5-FU on proliferation and apoptosis in biliary tract cancer)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

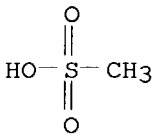
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 26 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:789131 CAPLUS
TI Determination of drug synergism between the tyrosine kinase inhibitors NSC 680410 (adaphostin) and/or STI571 (imatinib mesylate, Gleevec) with cytotoxic drugs against human leukemia cell lines
AU Avramis, Ioannis A.; Laug, Walter E.; Sausville, Edward A.; Avramis, Vassilios I.
CS Department of Pediatrics, Division of Hematology/Oncology, USC Keck School of Medicine, Los Angeles, CA, 90027, USA
SO Cancer Chemotherapy and Pharmacology (2003), 52(4), 307-318
CODEN: CCPHDZ; ISSN: 0344-5704
PB Springer-Verlag
DT Journal
LA English
AB The primary growth factor receptors involved in angiogenesis and lymphomagenesis can be grouped into the vascular endothelial growth factor (VEGF) receptors and related families. Inhibition of VEGF and other growth factors, including c-Abl, c-Kit, **platelet**-derived growth factor (PDGF), epidermal growth factor (EGF) and insulin-like growth factor (IGF), or their receptors containing tyrosine kinase domains by antiangiogenesis drugs disrupts cell survival signal transduction pathways and may contribute to the proapoptotic pathways in malignant cells. However, clin. trials suggest that signal transduction inhibitors have considerable antitumor activity when used as single agents only for a short time, most likely due to the development of drug resistance by the host or by the tumor cells. In order to prevent this problem and to augment their antitumor efficacy, these agents could be administered in combination with cytotoxic antineoplastic drugs. We hypothesized that the combination of the antiangiogenesis tyrosine kinase inhibitors with cytotoxic drugs would produce synergistic drug regimens. Two human T-lymphoblastic leukemia cell lines that express VEGF-R1, CEM/0 (wild-type, WT) and the drug-resistant clone CEM/ara-C/I/ASNase-0.5-2, were utilized in the drug combination studies. NSC 680410, a tyrosine kinase inhibitor given at 0.1 to 1 μM for 72 h, inhibited VEGF secretion and leukemic cell growth at 90% of vehicle-treated control cultures with an IC50 value of less than 1 μM. The cytotoxic drugs idarubicin (IDA), fludarabine (Fludara), and cytosine arabinoside (ara-C) were used for the various drug combinations. One-, two-, three-, and four-drug treatments were tested. Cell viability was documented by the MTT assay and photomicrog. estimation of apoptotic cells. Both the combination index (CI) and isobologram evaluations demonstrated strong synergism between these drugs and the tyrosine kinase inhibitor. NSC 680410 was highly synergistic with IDA, IDA + ara-C, and IDA + Fludara + ara-C, over

the resp. cytotoxic drug regimens at concns. easily achieved in patient plasma. NSC 680410 potentiated the activity of IDA in both leukemia cell lines by 17.8- and 221.4-fold in the WT and drug-resistant line, resp. The activity of NSC 680410 + IDA + ara-C was also potentiated by 58.8-fold in the WT line, and the activity of NSC 680410 + IDA + Fludara + ara-C by 2.4- and 6.47+106-fold in the WT and drug-resistant lines, resp. The results suggest that IDA was not needed for optimal synergistic activity in the CEM/0 cells, but IDA was a necessary component to obtain drug synergism in the drug-resistant clone. Similarly, STI571 (imatinib mesylate, Gleevec), the p210bcr/abl tyrosine kinase inhibitor, demonstrated synergism with Fludara + ara-C or IDA + ara-C. Most importantly STI571 showed synergism with NSC 680410, suggesting that these drugs inhibit different tyrosine kinase domains in human leukemia cells. Lastly, pretreatment of leukemic cells with NSC 680410 showed additivity with gamma radiation in comparison to either treatment modality alone. The data, taken together, suggest that by inhibiting the pro-survival signal transduction pathway (VEGF-R1) and DNA replication by cytotoxic drugs, leukemic cells undergo apoptosis in a synergistic manner. In conclusion, the combinations of antiangiogenesis and DNA-damaging cytotoxic drugs are highly synergistic regimens in both WT and drug-resistant leukemic cell lines and they should be examined further.

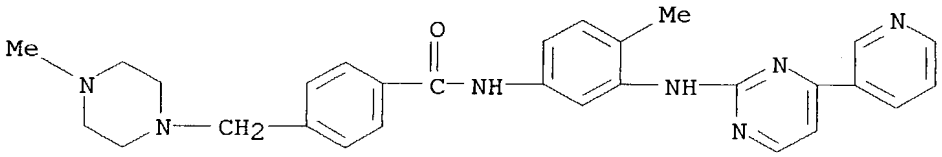
IT **220127-57-1**, STI571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergism between tyrosine kinase inhibitors NSC680410 (adaphostin) and/or STI571 (imatinib mesylate, Gleevec) with cytotoxic drugs against human leukemia cell lines)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

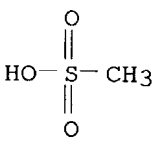
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

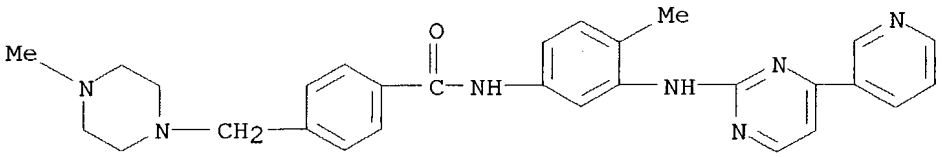


RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 27 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:780181 CAPLUS
DN 139:362622
TI Gain-of-function mutations of **platelet**-derived growth factor receptor α gene in gastrointestinal stromal tumors
AU Hirota, Seiichi; Ohashi, Akiko; Nishida, Toshirou; Isozaki, Koji; Kinoshita, Kazuo; Shinomura, Yasuhisa; Kitamura, Yukihiko
CS Department of Pathology, Osaka University Medical School, Suita, Japan
SO Gastroenterology (2003), 125(3), 660-667
CODEN: GASTAB; ISSN: 0016-5085
PB W. B. Saunders Co.
DT Journal
LA English
AB Most gastrointestinal stromal tumors (GISTs) have gain-of-function mutations of c-kit receptor tyrosine kinase (KIT) gene, but some GISTs do not. We investigated the cause of GISTs without KIT mutations. Because GISTs apparently expressed **platelet**-derived growth factor receptor (PDGFR) α, the authors examined whether GISTs without KIT mutations had a mutation of PDGFR α. Whole coding region of PDGFR α complementary DNA (cDNA) was sequenced in GISTs with or without KIT mutations. Mutant PDGFR α cDNA was transfected into 293T human embryonic kidney cells, and autophosphorylation of PDGFR α was examined Proliferation of Ba/F3 murine lymphoid cells stably transfected with mutant PDGFR α cDNA was estimated by tritium thymidine incorporation. Wild-type KIT cDNA was cotransfected with mutant PDGFR α cDNA, and immunopptn. by anti-KIT antibody was performed. Inhibitory effect of Imatinib mesylate on activated PDGFR α was examined We found 2 types of constitutively activated mutations of PDGFR α, Val-561 to Asp or Asp-842 to Val, in 5 of 8 GISTs without KIT mutations but not in 10 GISTs with KIT mutations. Stable transfection of each mutation induced autonomous proliferation of Ba/F3 cells. Constitutively activated mutant PDGFR α bound and activated the cotransfected wild-type KIT. The constitutive activation of PDGFR α with Val-561 to Asp was inhibited effectively by Imatinib mesylate but that of PDGFR α with Asp-842 to Val was inhibited only weakly, even at the concentration of 10 μmol/L. The gain-of-function mutations of PDGFR α appear to play an important role in development of GISTs without KIT mutations.
IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Imatinib mesylate effect on gastrointestinal stromal tumors with PDGFR gain-of-function mutations)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

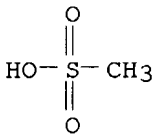
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 28 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:778806 CAPLUS
DN 140:263897
TI Imatinib mesylate elicits positive clinical response in atypical chronic myeloid leukemia involving the **platelet**-derived growth factor receptor beta
AU Garcia, Juan L.; de Mora, Jaime Font; Hernandez, Jesus M.; Queizan, Jose A.; Gutierrez, Norma C.; Hernandez, Jose M.; Miguel, Jesus F. San
CS Spain
SO Blood (2003), 102(7), 2699-2700
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB A patient with atypical chronic myeloid leukemia and t(5;10) translocation achieved a clin. and cytogenetic response after imatinib mesylate therapy. This translocation creates a H4(D10S170)/**platelet**-derived growth factor receptor beta (PDGFβR) fusion transcript. Based on the presence of PDGFβR rearrangement, the patient began treatment with imatinib at a daily dose of 400 mg. Clin. and cytogenetic complete response to imatinib was achieved after 3 wk of therapy. The patient remains in complete response after 1 yr of therapy.
IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate elicits treatment of atypical chronic myeloid leukemia involving a translocation creating the H4(D10S170)/**platelet**-derived growth factor receptor beta fusion transcript)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
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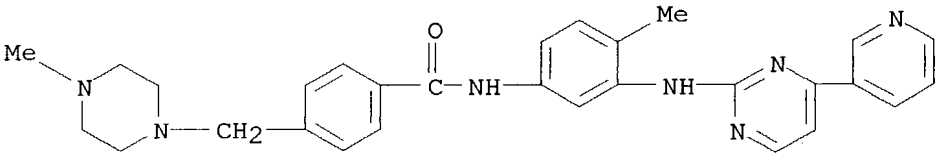

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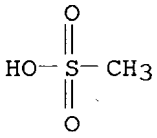


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 29 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:777593 CAPLUS
DN 139:271094
TI Inhibition of cell death responses induced by oxidative stress
IN Kufe, Donald W.; Kaddurah-Daouk, Rima
PA Dana-Farber Cancer Institute, Inc., USA
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003080061	A1	20031002	WO 2003-US10112	20030320

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-366410PP 20020321

AB The invention provides methods of reducing or preventing oxidative stress-induced cell death by contacting a cell with a compound that inhibits the kinase activity and/or the mitochondrial translocation of c-Abl. The methods of the invention can be used to treat individuals individual

diagnosed as having or being at risk of contracting a disorder characterized by excessive oxidative stress-induced cell death.

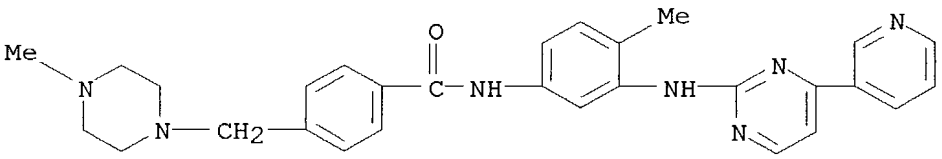
IT **220127-57-1**, STI571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of cell death responses to oxidative stress by inhibiting kinase or mitochondrial translocation of c-Abl for treatment of neurol. disorders and ischemia/reperfusion injury in combination with other drugs)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



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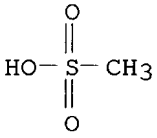

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 30 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:757504 CAPLUS
DN 139:271054
TI Imatinib for treating angiotensin II-mediated diseases
IN Gilbert, Richard Ernest; Kelly, Darren James; Feldman, David Louis
PA Novartis A.-G., Switz.; The University of Melbourne
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003077892	A2	20030925	WO 2003-EP2709	20030314

WO 2003077892 A3 20031224
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR
GB 2002-6216 A 20020315
GB 2002-6217 A 20020315
GB 2002-17505 A 20020729

OS MARPAT 139:271054

AB A PDGF receptor tyrosine kinase inhibitor, especially 4-(4-methylpiperazin-1-ylmethyl)-N-[[4-methyl-3-(4-pyridin-3-yl)pyrimidin-2-ylamino]phenyl]benzamide (I) or a pharmaceutically acceptable salt can be used in the treatment of angiotensin II-induced diseases and a combination which comprises (a) a PDGF receptor tyrosine kinase inhibitor, an antihypertensive, an aldosterone antagonist, an aldosterone synthase inhibitor and/or an angiotensin receptor blocker agent and optionally at least one pharmaceutically acceptable carrier for simultaneous, sep. or sequential use, in particular for the treatment of hypertension and hypertension-induced diseases. Imatini9b had no effect on systolic blood pressure but significantly reduced mesenteric weight in animals receiving angiotensin II. Pharmaceutical formulations of Imatinib were given.

IT **220127-57-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Imatinib for treating angiotensin II-mediated diseases)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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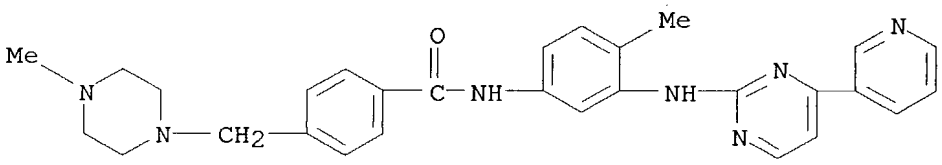
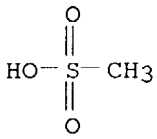


CM 2

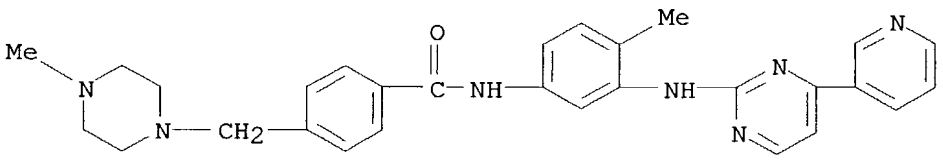
CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 31 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:741734 CAPLUS
DN 140:22896
TI STI-571 inhibits in vitro angiogenesis
AU Dudley, Andrew; Gilbert, Richard E.; Thomas, David; Cox, Alison; Price, John T.; Best, James; Jenkins, Alicia
CS St. Vincent's Hospital, Department of Medicine, University of Melbourne, Australia
SO Biochemical and Biophysical Research Communications (2003), 310(1), 135-142
CODEN: BBRCA9; ISSN: 0006-291X
PB Elsevier Science
DT Journal
LA English
AB Compds. that block angiogenesis are effective in the treatment of certain cancers and other angiogenesis-related diseases. Many of these compds. specifically target the rapidly proliferating and migrating endothelial cell. However, angiogenesis is a multi-faceted process involving heterotypic interactions between various cell types. For example, PDGFBB is an important cytokine secreted by endothelial cells that attracts smooth muscle cells to surround and stabilize a nascent vessel. Therefore, we hypothesized that STI-571, a tyrosine kinase inhibitor with PDGFβ receptor activity, would inhibit angiogenesis through an anti-migratory effect on smooth muscle cells. We demonstrate that STI-571 completely inhibits in vitro angiogenesis in fibrinogen-embedded mouse aorta. Furthermore, this angiostatic property was due mainly to an anti-migratory and anti-proliferative effect upon smooth muscle cells. These data suggest that STI-571, in addition to its efficacy in the treatment of certain cancers, may also prove to be clin. useful in diseases characterized by unregulated angiogenesis.
IT **220127-57-1**, STI-571
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI-571 inhibits in vitro angiogenesis)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

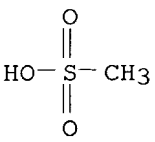
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



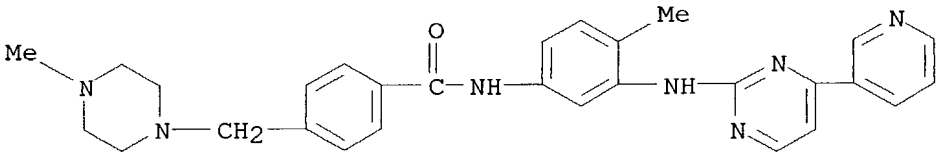
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 32 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:736046 CAPLUS
DN 140:192366
TI Expression of Kit and **platelet**-derived growth factor receptors α and β in cholangiocarcinoma, and case report of therapy with imatinib mesylate (STI571)
AU Holcombe, Randall F.; Gu, Mai; Imagawa, David; Milovanovic, Tatjana
CS Division of Hematology/Oncology, University of California and Chao Family Comprehensive Cancer Center, Irvine, CA, USA
SO Anti-Cancer Drugs (2003), 14(8), 651-657
CODEN: ANTDEV; ISSN: 0959-4973
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB We have evaluated the expression of Kit, a receptor encoded by the c-kit protooncogene, and **platelet**-derived growth factor-receptors (PDGF-R) α and β in cholangiocarcinoma specimens from 13 sep. patients, and provide a case report of a therapeutic trial of imatinib mesylate in one patient. Archived pathol. samples from 13 patients with cholangiocarcinoma were obtained. Tissue sections were hybridized with anti-Kit, anti-PDGF-Rα and anti-PDGF-Rβ monoclonal antibodies. Kit, PDGF-Rα and PDGF-Rβ expression was seen in 31, 69 and 46% of samples, resp. All patients with PDGF-Rβ expression also expressed PDGF-Rα. Three out of four patients with Kit expression did not express either PDGF receptor and only one patient exhibiting expression of PDGF expressed Kit. Cohen's κ statistic demonstrated that PDGF and Kit expression were inversely correlated with borderline significance (p=0.052; κ=-0.4742, 95% confidence interval -0.9821 to 0.03364). In one case, strong Kit expression was noted in a tumor from a metastatic lymph node, but was absent in the primary tumor, suggesting that Kit may be related to invasive or metastatic potential. Given the high level of expression defined in this study, a prospective clin. trial incorporating imatinib mesylate, alone or in combination with cytotoxic chemotherapy, and especially in chemotherapy-naive patients, should be considered for patients with cholangiocarcinoma.
IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(expression of Kit and PDGF receptors in cholangiocarcinoma and therapy with imatinib mesylate)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-

pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

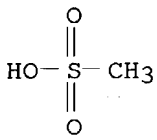
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 33 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:733890 CAPLUS
DN 140:121825
TI Target-based therapy against gastrointestinal stromal tumors - from molecular diagnosis to molecular target therapy
AU Nishida, Toshirou; Yasumasa, Keigo
CS Dept. of Surgery, Osaka University Graduate School of Medicine, Japan
SO Gan to Kagaku Ryoho (2003), 30(8), 1071-1078
CODEN: GTKRDX; ISSN: 0385-0684
PB Gan to Kagaku Ryohosha
DT Journal; General Review
LA Japanese
AB A review. Gastrointestinal stromal tumors (GIST) are composed of KIT-pos. mesenchymal-origin spindle-or polygonal-shaped tumor cells in the gastrointestinal tract without immunoreactivity for desmin and S-100. The gain-of-function mutations in the c-kit gene (90%) or **platelet** -derived growth factor receptorα (PDGF-Rα) gene (5%) are now considered to be causative for GIST. ST1571 (Glivec), a mol. designed to selectively inhibit Bcr-Abl, KIT, and PDGF-R activity, shows high response rate and efficacy for non-resectable and/or relapsed GIST (PR 60%). Its serious adverse effects (more than Grade 3) were infrequent, thus, tolerability and safety are good. Glivec is the first successful case of mol. target therapy for solid tumors. However, new resistance against this new generation of drug is going to appear and becomes an urgent problem.

IT **220127-57-1**, Glivec
RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(target-based therapy against gastrointestinal stromal tumors - from mol. diagnosis to mol. target therapy)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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CRN 152459-95-5
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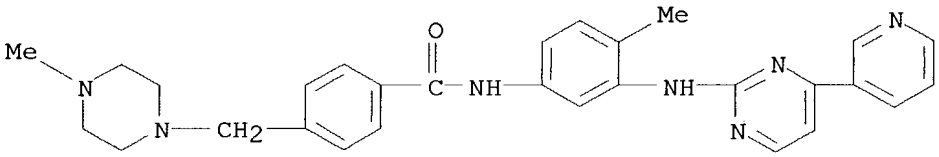
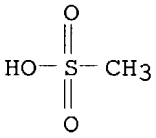


CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 34 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:733889 CAPLUS
DN 140:121824
TI Molecular-target therapy of Ph-positive leukemia by imatinib (tyrosine kinase inhibitor)
AU Tauchi, Tetsuzo; Ohyashiki, Kazuma
CS First Dept. of Internal Medicine, Tokyo Medical University, Japan
SO Gan to Kagaku Ryoho (2003), 30(8), 1065-1070
CODEN: GTKRDX; ISSN: 0385-0684
PB Gan to Kagaku Ryohosha
DT Journal; General Review
LA Japanese
AB A review. Imatinib mesylate is a 2-phenylaminopyrimidine tyrosine kinase inhibitor with specific activity for ABL, **platelet**-derived growth factor receptor, and c-kit receptor. The pharmacol. basis of this interaction has been elucidated by crystallog. studies. Imatinib mesylate binds to the amino acids of the BCR-ABL tyrosine kinase ATP binding site and stabilizes the inactive, non-ATP-binding form of BCR-ABL, thereby preventing tyrosine autophosphorylation, and in turn, phosphorylation of its substrates. This process ultimately results in a "switch-off" of the

downstream signaling pathways that promote leukemogenesis. Despite high rates of hematol. and cytogenetic responses to imatinib therapy, the emergence of resistance to imatinib has been recognized as a major problem in the treatment of Ph-pos. leukemia. Considerable progress has been made in developing therapeutic agents that are effective against mol. targets specifically expressed in CML cells. It is important to emphasize that BCR-ABL is the ideal target for therapy even at relapse; at least one general mechanism of resistance involves maintenance of an active BCR-ABL kinase inside leukemic cells. It is also notable that the high frequency of BCR-ABL mutations and amplifications represents the high degree of heterogeneity in patients with advanced CML, in whom multiple leukemic clones may exist. For these reasons, a single inhibitor is unlikely to be able to block all mutants described so far.

IT **220127-57-1**, Imatinib mesylate
RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol.-target therapy of Ph-pos. leukemia by imatinib (tyrosine kinase inhibitor))

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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CRN 152459-95-5
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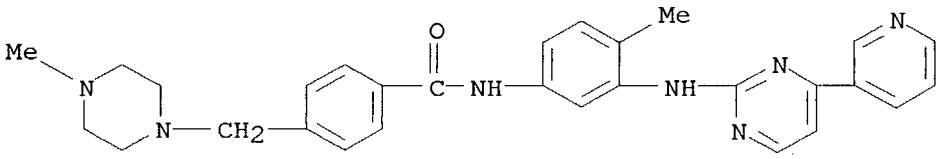
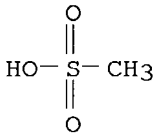


CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 35 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:701383 CAPLUS
DN 139:321144
TI Expression of c-ABL, c-KIT, and **platelet**-derived growth factor receptor-β in ovarian serous carcinoma and normal ovarian surface epithelium
AU Schmandt, Rosemarie E.; Broaddus, Russell; Lu, Karen H.; Shvartsman, Hyun;

Thornton, Angela; Malpica, Anais; Sun, Charlotte; Bodurka, Diane C.; Gershenson, David M.

CS Department of Gynecologic Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA

SO Cancer (New York, NY, United States) (2003), 98(4), 758-764
CODEN: CANCAR; ISSN: 0008-543X
PB John Wiley & Sons, Inc.
DT Journal
LA English

AB BACKGROUND. Tyrosine kinases, such as c-KIT, c-ABL, and **platelet**-derived growth factor-beta (PDGFR-β), are important regulators of cell growth. Highly potent and selective inhibitors of tyrosine kinases are being investigated as alternatives to standard chemotherapy. One such inhibitor, imatinib mesylate, is being used to treat gastrointestinal stromal tumors and chronic myelogenous leukemia. Ovarian carcinomas frequently develop resistance to conventional chemotherapeutic agents. Immunohistochem. expression of c-ABL, PDGFR-β, and c-KIT was evaluated in ovarian carcinomas to determine whether treatment with imatinib mesylate might be feasible. METHODS. The expression of c-ABL, c-KIT, and PDGFR-β in tumors was evaluated by immunohistochem. anal. of 52 ovarian serous carcinomas, including 21 low-grade (well differentiated) and 31 high-grade (poorly differentiated) tumors. Fourteen normal ovaries were also evaluated. RESULTS. In normal ovarian surface epithelium, c-ABL was expressed universally. PDGFR-β was expressed in the majority (93%) of samples of normal ovarian epithelium, whereas the c-KIT protein was undetectable in normal ovarian surface epithelium. Overall, c-ABL was expressed in 71% of serous carcinomas. C-ABL was expressed more frequently in the low-grade serous carcinomas (81%) compared with the high-grade serous carcinomas (65%). PDGFR-β expression was observed in 81% of serous carcinomas overall and was observed more frequently in higher-grade tumors. C-KIT immunohistochem. staining was absent in low-grade tumors but was present in 26% of high-grade serous carcinomas. CONCLUSIONS. The majority of ovarian serous carcinomas express one or more of the kinases targeted by the tyrosine kinase inhibitor, imatinib mesylate, suggesting the potential usefulness of this drug in the treatment of ovarian carcinoma.

IT **220127-57-1**, Imatinib mesylate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-ABL, c-KIT and PDGF receptor-β expressions in ovarian serous carcinoma and normal ovarian surface epithelium in relation to imatinib mesylate usefulness)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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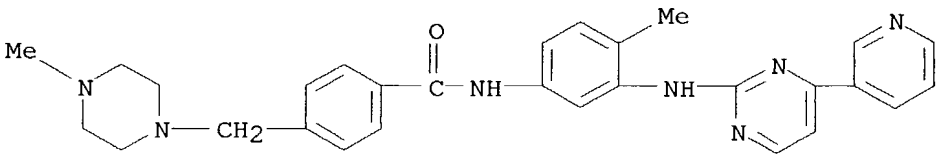
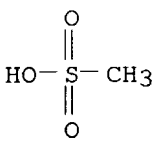


CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 36 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:695036 CAPLUS
DN 140:104241
TI Diagnosis and therapy of gastrointestinal stromal tumors from molecular diagnosis to molecular target therapy
AU Nishida, Toshirou; Endo, Shunji
CS Department of Surgery, Osaka University Graduate School of Medicine, Suita, 565-0871, Japan
SO Biotherapy (Tokyo, Japan) (2003), 17(4), 352-360
CODEN: BITPE9; ISSN: 0914-2223
PB Gan to Kagaku Ryohosha
DT Journal; General Review
LA Japanese
AB A review. Gastrointestinal stromal tumor (GIST), a very frequent type of gastrointestinal mesenchymal tumor, is defined by KIT-pos. mesenchymal-origin spindle-shaped cell tumors in the gastrointestinal tract (when KIT-neg., at least CD34 should be immunohistochem. pos.). The gain-of-function mutations in the c-kit gene (90%) or **platelet** -derived growth factor receptor α (PDGF-Rα) gene (5%) are now considered to be causative for GIST. STI571 (Gleevec), a mol. designed to inhibit Bcr-Abl, KIT, and PDGF-R activity, shows high response and efficacy in non-resectable and/or relapsed GIST (PR 50% and SD 25%). Its adverse effects are frequent but serious adverse effects (more than Grade 3) are infrequent, thus, tolerability and safety are good. Gleevec is the first successful case for mol. target therapy based on mol. diagnosis of GIST.
IT **220127-57-1**, Gleevec
RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnosis and therapy of gastrointestinal stromal tumors from mol. diagnosis to mol. target therapy)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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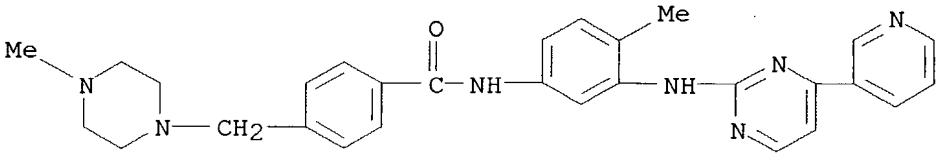
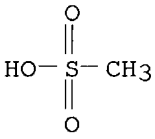
CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 37 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:690813 CAPLUS
DN 140:87216
TI Growth inhibition of rat osteosarcoma and malignant fibrous histiocytoma cells by tyrosine kinase inhibitor STI571
AU Yoshitani, Kazuhiro; Honoki, Kanya; Morishita, Toru; Kido, Akira; Miyauchi, Yoshizumi; Mii, Yoshio; Takakura, Yoshinori
CS Department of Orthopedic Surgery, Nara Medical University, Kashihara, Nara, 634-8522, Japan
SO In Vivo (2003), 17(3), 255-258
CODEN: IVIVE4; ISSN: 0258-851X
PB International Institute of Anticancer Research
DT Journal
LA English
AB STI571 is a 2-phenylaminopyrimide derivative that was designed as an Abl tyrosine kinase inhibitor, but it is also effective against **platelet**-derived growth factor receptor (PDGFR) and c-Kit tyrosine kinase. Recent studies have demonstrated that STI571 inhibits the growth of several tumors in which PDGF or c-kit play an important role in tumor pathogenesis. We have recently established rat osteosarcoma and malignant fibrous histiocytoma (MFH) cell lines. RT-PCR anal. revealed that MFH and osteosarcoma cell lines expressed high and very low levels of PDGFRα resp., and that all cell lines expressed similar levels of PDGFRβ. The level of c-kit mRNA expression were almost negligible in all cell lines. The effect of STI571 on cellular growth measured by MTS calorimetric dye reduction showed that the growth of each cell line was inhibited in a dose and time-dependent manner. STI571 (10 μM) inhibited the rates of cell growth of MFH cells by up to 40% and of osteosarcoma cells by only to 20% after 72 h. These data suggested that STI571 tyrosine kinase inhibitor plays a role in blocking or slowing the rate of growth of MFH and osteosarcoma cells expressing tyrosine kinase type receptor.
IT **220127-57-1**, STI571
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(growth inhibition of rat osteosarcoma and malignant fibrous

histiocytoma cells by tyrosine kinase inhibitor STI571)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
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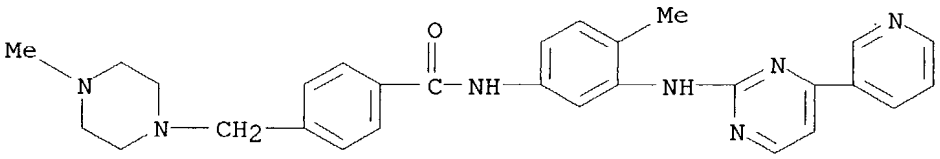
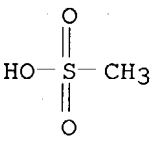


CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 38 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:670060 CAPLUS
DN 140:87200
TI Chronic myeloproliferative disorders with rearrangement of the **platelet**-derived growth factor α receptor: a new clinical target for STI571/Glivec
AU Trempat, Pascal; Villalva, Claire; Laurent, Guy; Armstrong, Florence; Delsol, Georges; Dastugue, Nicole; Brousset, Pierre
CS Centre de Physiopathologie de Toulouse-Purpan', INSERM U563, Department of Pathology, Purpan Hospital, Toulouse, Fr.
SO Oncogene (2003), 22(36), 5702-5706
CODEN: ONCNES; ISSN: 0950-9232
PB Nature Publishing Group
DT Journal
LA English
AB Two cases of atypical chronic myeloid leukemia (CML) carrying the t(4;22)(q12;q11) translocation involving the breakpoint cluster region (BCR) and **platelet**-derived growth factor α receptor (PDGFRA) genes have been recently characterized. We report a third case of atypical CML with the same translocation but with a distinct breakpoint fusing BCR exon 1 with PDGFRA exon 13. The patient had a clin. presentation of CML with progressive transformation in B-cell acute

lymphoblastic leukemia. The involvement of PDGFRA led us to treat the patient with the small organic compound Imatinib mesylate/STI571 (Glivec) that blocks the ATP binding site of tyrosine kinases such as Abelson, KIT and **platelet**-derived growth factor receptors. The patient subsequently achieved a rapid clin. and mol. response clearly demonstrating, for the first time, that Glivec is active against PDGFRA in vivo. Therefore, our study expands the list of Glivec targets and has direct biol. and also clin. implications.

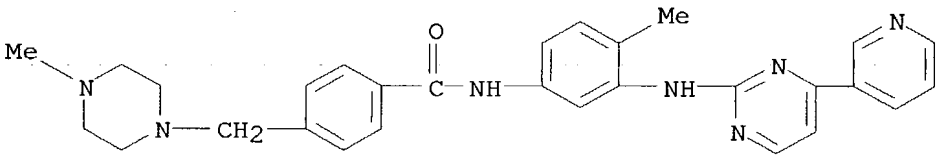
IT **220127-57-1**, STI571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic myeloproliferative disorders with rearrangement of the **platelet**-derived growth factor α receptor as a new clin. target for Glivec)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

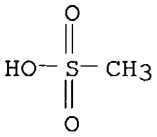
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 39 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:669373 CAPLUS
DN 140:246257
TI Anagrelide and imatinib mesylate combination therapy in patients with chronic myeloproliferative disorders
AU Tsimberidou, Apostolia M.; Colburn, Dawn E.; Welch, Mary Alma; Cortes, Jorge E.; Verstovsek, Srdan; O'Brien, Susan M.; Albitar, Maher; Kantarjian, Hagop M.; Giles, Francis J.
CS Department of Leukemia, M.D. Anderson Cancer Center, University of Texas,

Houston, TX, 77030, USA
SO Cancer Chemotherapy and Pharmacology (2003), 52(3), 229-234
CODEN: CCPHDZ; ISSN: 0344-5704
PB Springer-Verlag
DT Journal
LA English
AB The tyrosine kinase inhibitor imatinib mesylate inhibits the function of the Bcr-Abl oncoprotein associated with Philadelphia-pos. chronic myelogenous leukemia (CML). Anagrelide suppresses megakaryocyte proliferation and differentiation. The objectives of this study were to investigate the feasibility and safety of imatinib mesylate and anagrelide combination therapy in patients with Ph-pos. CML or chronic myeloproliferative disorders (MPD) with persistent thrombocythemia. This study was a retrospective review of all available records of patients with chronic MPD presenting to the M.D. Anderson Cancer Center between Oct. 1998 and May 2002, treated with imatinib mesylate combined with anagrelide. Of 22 patients identified, 18 had Ph-pos. CML (chronic phase, 16 patients; accelerated phase, 2 patients), 1 had agnogenic myeloid metaplasia (AMM), 2 had essential thrombocythemia (ET) and 1 had MPD transformed into refractory anemia with excess blasts (RAEB). The median age was 57 yr (range 26-82 yr). The median dose of imatinib mesylate administered was 400 mg (range 300-800 mg) and the median dose of anagrelide was 1.5 mg (range 0.5-4.0 mg). Imatinib mesylate and anagrelide combination therapy was feasible and tolerable. Of the 18 patients with Ph-pos. CML, 15 in chronic phase and 1 in accelerated phase achieved a complete hematol. response (CHR), and 9 of the 18 achieved cytogenetic response (complete in 8 patients). No responses were noted in patients with AMM, ET or MPD transformed into RAEB. The combination of imatinib mesylate and anagrelide was safe and was associated with an 89% CHR rate in patients with CML in chronic phase and persistent thrombocythemia.
IT **220127-57-1**, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anagrelide and imatinib mesylate combination therapy in patients with chronic myeloproliferative disorders)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
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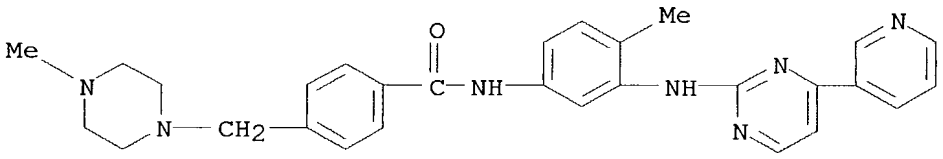

CM 2

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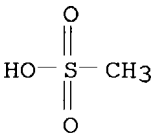


RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 40 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:633416 CAPLUS
DN 139:173786
TI Method for treating diseases associated with abnormal kinase activity
IN Lyons, John; Rubinfeld, Joseph
PA Supergen, Inc., USA
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003065995	A2	20030814	WO 2003-US3537	20030206
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
				US 2002-71849	A120020207
				US 2002-206854	A120020726
	US 2003147813	A1	20030807	US 2002-71849	20020207

PATENT FAMILY INFORMATION:
FAN 2003:609844

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003147813	A1	20030807	US 2002-71849	20020207
	WO 2003065995	A2	20030814	WO 2003-US3537	20030206
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
				US 2002-71849	A120020207
				US 2002-206854	A120020726

AB Methods are provided for treating diseases associated with abnormal activity of kinases such as chronic myelogenous leukemia. The method comprises: administering a DNA methylation inhibitor to the patient in therapeutically effective amount; and administering a kinase inhibitor such as imatinib mesylate to the patient in therapeutically effective amount, such that the in vivo activity of the kinase is reduced relative to that prior to the treatment. The method can be used to treat cancer associated with abnormal activity of kinases such as phosphatidylinositol 3'-kinase (P13K), protein kinases including serine/threonine kinases such as Raf kinases, protein kinase kinases such as MEK, and tyrosine kinases such as those in the epidermal growth factor receptor family (EGFR), **platelet**-derived growth factor receptor family (PDGFR), vascular endothelial growth factor receptor (VEGFR) family, nerve growth factor receptor family (NGFR), fibroblast growth factor receptor family (FGFR) insulin receptor family, ephrin receptor family, Met family, Ror family, c-kit family, Src family, Fes family, JAK family, Fak family, Btk family, Syk/ZAP-70 family, and Abl family.

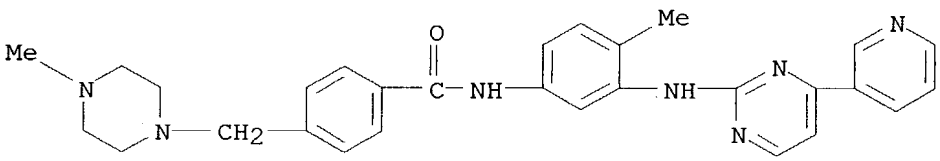
IT **220127-57-1**, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of diseases associated with abnormal kinase activity such as chronic myelogenous leukemia with kinase inhibitor and DNA methylation inhibitor in relation to overcoming resistance and drug toxicity)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

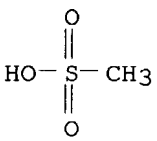
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 41 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:610603 CAPLUS

DN 139:159912
TI Sequences of mouse and human protein SUAP (small ubiquinated apoptotic protein) and uses in inducing growth arrest and apoptosis in cancer cells
IN Baker, Stacey Jill; Reddy, E. Premkumar
PA Temple University - of the Commonwealth System of Higher Education, USA
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003064616	A2	20030807	WO 2003-US2942	20030131

PI
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-353622PP 20020131

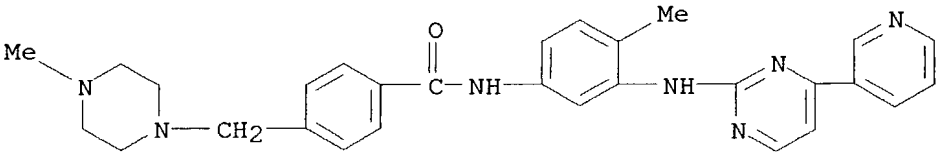
AB Growth arrest and apoptosis in cells can be induced in cells which are resistant to apoptosis with SUAP (small ubiquinated apoptotic protein) and derivs., homologs and analogs of SUAP. Detection of endogenous SUAP expression can also be used as a marker of apoptosis in cells undergoing apoptosis-inducing therapeutic treatments. The invention provides protein and cDNA sequences of mouse and human protein SUAP (small ubiquinated apoptotic protein). SUAP RNA was highly expressed in multiple tissues, including **heart**, brain, testis, liver and kidney. SUAP expression was also observed in lung and spleen, albeit to a lesser extent. Endogenous SUAP was unstable and was subject to degradation by proteosome. SUAP was up-regulated during G-CSF-induced terminal differentiation of 32Dcl3 cells and IL-3 withdrawal-induced apoptosis of 32Dcl3. SUAP RNA was induced in MCF7 cells in response to serum-withdrawal-induced apoptosis; taxol-induced apoptosis; etoposide-induced apoptosis; cisplatin-induced apoptosis. SUAP RNA was induced in response to irradiation of DU145 and LnCap prostate tumor cells; androgen ablation of LnCap cells; and irradiation of androgen depleted LnCap cells.

IT **220127-57-1**, STI571
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as external apoptosis inducing-stimulus; sequences of mouse and human protein SUAP (small ubiquinated apoptotic protein) and uses in inducing growth arrest and apoptosis in cancer cells)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

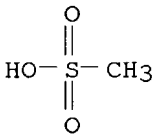
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 42 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:609844 CAPLUS
DN 139:128007
TI Method for treating chronic myelogenous leukemia combined with some resistance to imatinib mesylate using DNA methylation inhibitor to mitigate imatinib mesylate resistance
IN Lyons, John
PA USA
SO U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003147813	A1	20030807	US 2002-71849	20020207
	WO 2003065995	A2	20030814	WO 2003-US3537	20030206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-71849 A120020207
US 2002-206854 A120020726

PATENT FAMILY INFORMATION:
FAN 2003:633416

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003065995	A2	20030814	WO 2003-US3537	20030206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-71849 A120020207
US 2002-206854 A120020726

US 2003147813 A1 20030807 US 2002-71849 20020207

AB Methods, compns. and kits are provided for treating cancer associated with protein tyrosine kinase activity such as chronic myelogenous leukemia. In particular, a treatment method is provided comprising: administering to a patient having chronic myelogenous leukemia and a degree of resistance to imatinib mesylate, a therapeutically effective amount of a DNA methylation inhibitor which mitigates the imatinib mesylate resistance.

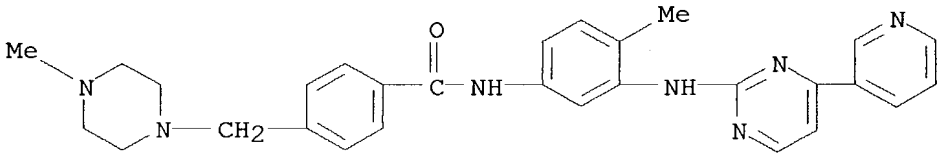
IT **220127-57-1**, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating chronic myelogenous leukemia combined with some resistance to imatinib mesylate using DNA methylation inhibitor to mitigate imatinib mesylate resistance)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

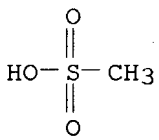
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 43 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:553747 CAPLUS
DN 139:162919
TI Mesenchymal chondrosarcoma: molecular characterization by a proteomic approach, with morphogenic and therapeutic implications
AU Brown, Robert E.; Boyle, Jenny L.
CS Division of Laboratory Medicine, Geisinger Medical Center, Danville, PA, USA
SO Annals of Clinical and Laboratory Science (2003), 33(2), 131-141
CODEN: ACLSCP; ISSN: 0091-7370
PB Association of Clinical Scientists
DT Journal
LA English
AB This study characterizes 3 cases of mesenchymal chondrosarcoma (MC) utilizing a proteomic approach that allows for the detection, visual quantification, cellular compartmentalization, and assessment of the functional state of certain proteins that may promote tumor growth and/or oppose apoptosis. Immunohistochem. procedures were performed to detect the following protein antigens: CD99, interleukin (IL)-1α, IL-6, transforming growth factor (TGF)-α, conventional (c) protein kinase C (cPKC)-α, cPKC-βII, phosphorylated (p)-PKC-α/βII, c-kit (CD117), **platelet**-derived growth factor receptor (PDGFR)-α, PDGFR-β, epidermal growth factor receptor (EGFR), human epidermal growth factor receptor (HER)-2/neu, cathepsin D, angiotensin-converting enzyme (ACE), angiotensin II type 1 (AT1) receptor, p21ras, the a subunit of farnesyl and geranylgeranyl transferase (FTα/GGTα), phospho (p)-c-Jun N-terminal kinase (p-JNK), p-p38 mitogen-activated protein kinase (MAPK), cyclin D1, c-Jun, Ki-67, bcl-2, TGF-β1 latency-associated peptide (LAP), TGF-βRII, and cyclooxygenase (COX)-2. Immunoreactivities were scored from 0 to 3+ positivity using bright-field microscopy. The results showed that malignant mesenchymal chondroblasts exhibit stronger expressions of CD99, IL-1α, cPKC-α, p-PKC-α/βII, PDGFR-α, p-JNK, Ki-67, and bcl-2 antigens than their more mature-appearing chondrocytic counterparts in MC. In conclusion, mol. profiling of mesenchymal chondrosarcoma using a proteomic approach characterized the mesenchymal chondroblasts as possessing pathways that incorporate PKC-α and PDGFR-α signaling and anti-apoptotic bcl-2 expression. Specific therapies to target the mesenchymal chondroblasts in mesenchymal chondrosarcoma might include interferon-α, rapamycin, ciprofloxacin, and STI571.
IT **220127-57-1**, STI571
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mesenchymal chondrosarcoma, mol. characterization by a proteomic approach, with morphogenic and therapeutic implications)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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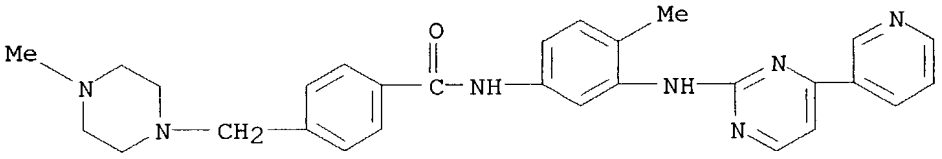
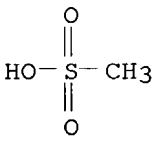
CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 44 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:551338 CAPLUS
DN 139:111702
TI Compositions and methods using ATP-dependent γ-secretase modulators for prevention and treatment of amyloid-β peptide-related disorders, and screening methods for modulators of Aβ
IN Netzer, William J.; Greengard, Paul; Xu, Huaxi
PA The Rockefeller University, USA
SO PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003057165	A2	20030717	WO 2003-US249	20030106
	WO 2003057165	A3	20031113		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

				US 2002-345009PP	20020104
	US 2004028673	A1	20040212	US 2003-337261	20030106
				US 2002-345009PP	20020104

OS MARPAT 139:111702
AB The invention provides methods and compns. for modulating levels of amyloid-β peptide (Aβ) exhibited by cells or tissues. The

invention also provides pharmaceutical compns. and methods of screening for compds. that modulate Aβ levels. The invention also provides modulation of Aβ levels via selective modulation (e.g., inhibition) of ATP-dependent γ-secretase activity. The invention also provides methods of preventing, treating or ameliorating the symptoms of a disorder, including but not limited to an Aβ-related disorder, by administering a modulator of γ-secretase, including, but not limited to, a selective inhibitor of ATP-dependent γ-secretase activity or an agent that decreases the formation of active (or optimally active) γ-secretase. The invention also provides the use of inhibitors of ATP-dependent γ-secretase activity to prevent, treat or ameliorate the symptoms of Alzheimer's disease.

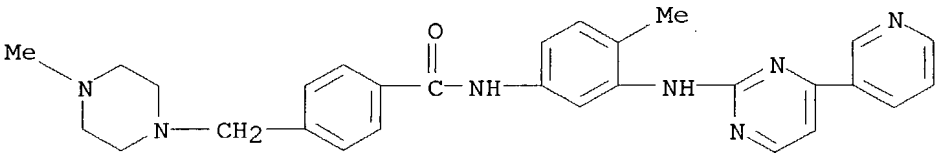
IT **220127-57-1**, STI 571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ATP-dependent enzyme modulators for prevention and treatment of amyloid-β peptide-related disorders, and screening methods for modulators of Aβ)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

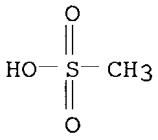
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

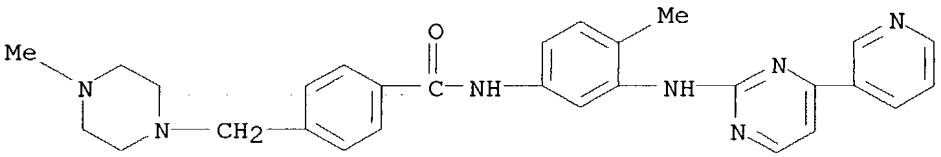


L17 ANSWER 45 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:534665 CAPLUS
DN 139:159339
TI Drugs targeted against protein kinases. [Erratum to document cited in CA137:56743]
AU Kumar, C. Chandra; Madison, Vincent
CS Departments of Tumour Biology and Structural Chemistry, Schering-Plough

Research Institute, Kenilworth, NJ, 07033, USA
SO Expert Opinion on Emerging Drugs (2002), 7(1), 207
CODEN: EOEDA3
PB Ashley Publications Ltd.
DT Journal; General Review
LA English
AB A review. In Table 1 under Company, Zymogenetics should be Celltech. Although the PDGF-beta target was originated by Zymogenetics, it is exclusively licensed to Celltech. The corrected table is given.
IT **220127-57-1**, Gleevec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; anticancer drugs targeted against protein kinases (Erratum))
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

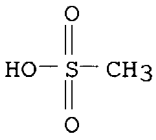
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 46 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:528874 CAPLUS
DN 139:159337
TI Imatinib: a targeted clinical drug development
AU Capdeville, Renaud; Silberman, Sandra
CS Novartis Oncology, Novartis Pharma AG, Basel, Switz.
SO Seminars in Hematology (2003), 40(2, Suppl. 2), 15-20
CODEN: SEHEA3; ISSN: 0037-1963
PB W. B. Saunders Co.
DT Journal; General Review
LA English
AB A review. Imatinib (Gleevec) (formerly STI571) is an orally bioavailable

rationally developed inhibitor of the tyrosine kinases Bcr-Abl, Kit, and **platelet**-derived growth factor receptor (PDGFR). In 4 yr of clin. development, more than 12,000 patients have been treated in the clin. development program. Imatinib was first shown to be highly effective in the treatment of all stages of chronic myelogenous leukemia (CML). Moreover, preliminary results of a randomized study have demonstrated superior efficacy and safety of first-line imatinib therapy compared with a combination of interferon and cytarabine. Imatinib has also been shown to be the only effective drug therapy in the treatment of patients with metastatic gastrointestinal stromal tumors expressing the stem cell factor (SCF) receptor Kit. This review outlines the successive steps in the clin. development of this new, targeted anticancer agent.

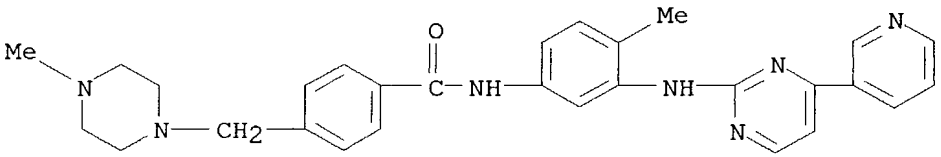
IT **220127-57-1**, STI571
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. development of imatinib (formerly STI571) in treatment of chronic myelogenous leukemia (CML))

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



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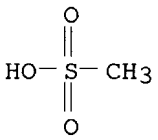


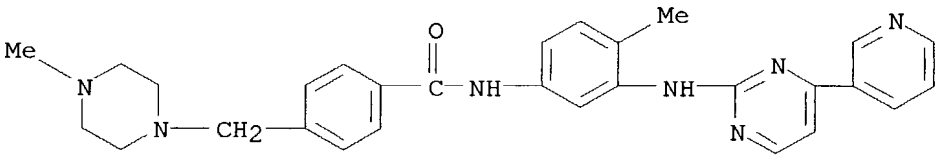
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 47 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:521932 CAPLUS
DN 139:147708
TI Discovery of a fusion kinase in EOL-1 cells and idiopathic hypereosinophilic syndrome
AU Griffin, John H.; Leung, Joey; Bruner, Rebecca J.; Caligiuri, Michael A.;

Briesewitz, Roger
CS Theravance, Inc., South San Francisco, CA, 94080, USA
SO Proceedings of the National Academy of Sciences of the United States of America (2003), 100(13), 7830-7835
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Idiopathic hypereosinophilic syndrome (HES) is a myeloproliferative disease of unknown etiol. Recently, it has been reported that imatinib mesylate (Gleevec), an inhibitor of Bcr-Abl kinase useful in the treatment of chronic myeloid leukemia, is also effective in treating HES; however, the mol. target of imatinib in HES is unknown. This report identifies a genetic rearrangement in the eosinophilic cell line EOL-1 that results in the expression of a fusion protein comprising an N-terminal region encoded by a gene of unknown function with the GenBank accession number NM_030917 and a C-terminal region derived from the intracellular domain of the **platelet**-derived growth factor receptor α (PDGFRα).
The fusion gene was also detected in blood cells from two patients with HES. The authors propose naming NM_030917 Rhe for Rearranged in hypereosinophilia. Rhe-PDGFRα fusions result from an apparent interstitial deletion that links Rhe to exon 12 of PDGFRα on chromosome 4q12. The fusion kinase Rhe-PDGFRα is constitutively phosphorylated and supports IL-3-independent growth when expressed in BaF3 cells. Proliferation and viability of EOL-1 and BaF3 cells expressing Rhe-PDGFRα are ablated by the PDGFRα inhibitors imatinib, vatalanib, and THRX-165724.
IT **220127-57-1**, Gleevec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discovery of fusion kinase in EOL-1 cells and idiopathic hypereosinophilic syndrome in relation to proliferation/viability ablation by)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

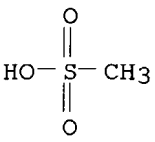
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 48 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:511932 CAPLUS
DN 139:65742
TI Method of using optical interrogation to determine a biological property of a cell or population of cells
IN Chung, Thomas D. Y.; Forster, Anita; Hall, Jeff; Kariv, Ilona; Lykstad, Kris; Schnabel, Catherine A.; Soo, Hoo William; Diver, Jonathan
PA Genoptix, Inc., USA
SO U.S. Pat. Appl. Publ., 71 pp., Cont.-in-part of U.S. Ser. No. 53,507.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 20

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US 2004053209 A1 20040318 US 2002-326885 20021219
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WO 2003093496 A1 20031113 WO 2003-US13735 20030430
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US 2002-377145PP 20020501
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US 2002-324926 A 20021219
US 2003-427748 A 20030429

PATENT FAMILY INFORMATION:

FAN 2002:368758

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2000-248451PP 20001113
US 2001-843902 A 20010427
AU 2002030696 A5 20020521 AU 2002-30696 20011109
US 2000-248451PP 20001113
US 2001-843902 A 20010427
WO 2001-US47421W 20011109
EP 1334355 A1 20030813 EP 2001-990939 20011109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
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US 2001-843902 A 20010427
WO 2001-US47421W 20011109

FAN 2002:610486

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PI	US 2002108859	A1	20020815	US 2001-993389	20011114
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	US 2003007894	A1	20030109	US 2001-845245 20010427

FAN 2002:638213

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PI	US 2002115164	A1	20020822	US 2001-993377 20011114
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	US 2003007894	A1	20030109	US 2001-845245 20010427
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	US 2003124516	A1	20030703	US 2002-243611 20020912
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				US 2002-377145PP 20020501
				US 2002-399931PP 20020730
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FAN 2002:638367

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PI	US 2002113204	A1	20020822	US 2001-993388 20011114
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	US 2003007894	A1	20030109	US 2001-845245 20010427

FAN 2002:638405

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PI	US 2002115163	A1	20020822	US 2001-993317 20011114
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FAN 2002:674431

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PI	US 2002121443	A1	20020905	US 2001-993378 20011114
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	US 2003007894	A1	20030109	US 2001-845245 20010427

FAN 2002:674682

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PI	US 2002123112	A1	20020905	US 2001-993375 20011114
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	US 2003007894	A1	20030109	US 2001-845245 20010427

FAN 2002:716953

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PI	US 2002132315	A1	20020919	US 2001-993326 20011114
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FAN 2002:716954

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PI US 2002132316	A1	20020919	US 2001-993376	20011114
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US 2003007894	A1	20030109	US 2001-845245	20010427

FAN 2002:833618

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US 2003124516	A1	20030703	US 2002-243611	20020912
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WO 2003062867	A2	20030731	WO 2003-US340	20030106
WO 2003062867	A3	20031204		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

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US 2002-53507 A 20020117

FAN 2003:21842

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PI US 2003008364	A1	20030109	US 2001-993318	20011114
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FAN 2003:23333

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				US 2002-399931PP 20020730
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FAN 2003:818057

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FAN 2003:892326

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FAN 2003:892941

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PI	WO 2003093496	A1	20031113	WO 2003-US13735	20030430

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				US 2002-324926 A	20021219
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FAN 2004:34161

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				US 2003-427748 A 20030429

FAN 2004:100664

	PATENT NO.	KIND	DATE	APPLICATION NO. DATE
PI	US 2004023310	A1	20040205	US 2002-326568 20021219
				US 2001-845245 A220010427
				US 2001-993377 A220011114
				US 2002-243611 A220020912
	US 2003007894	A1	20030109	US 2001-845245 20010427
	US 2002115164	A1	20020822	US 2001-993377 20011114
				US 2000-248451PP 20001113
				US 2001-845245 A220010427
	US 2003124516	A1	20030703	US 2002-243611 20020912
				US 2001-845245 A220010427
				US 2001-993377 A220011114
				US 2002-53507 A220020117

FAN 2004:142690

	PATENT NO.	KIND	DATE	APPLICATION NO. DATE
PI	US 2004033539	A1	20040219	US 2003-427748 20030429
				US 2002-377145PP 20020501
				US 2002-399931PP 20020730
				US 2002-400936PP 20020801
				US 2002-243611 A220020912
				US 2002-324926 A220021219
	US 2003124516	A1	20030703	US 2002-243611 20020912
				US 2001-845245 A220010427
				US 2001-993377 A220011114
				US 2002-53507 A220020117

US 2004009540 A1 20040115 US 2002-324926 20021219
US 2001-845245 A220010427
US 2002-377145PP 20020501
US 2002-399931PP 20020730
US 2002-400936PP 20020801
US 2002-243611 A220020912
WO 2003093496 A1 20031113 WO 2003-US13735 20030430
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002-377145PP 20020501
US 2002-399931PP 20020730
US 2002-400936PP 20020801
US 2002-243611 A 20020912
US 2002-324926 A 20021219
US 2003-427748 A 20030429

FAN 2004:219917

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004053209	A1	20040318	US 2002-326885	20021219
			US 2002-243611 A220020912	
US 2003124516	A1	20030703	US 2002-243611	20020912
			US 2001-845245 A220010427	
			US 2001-993377 A220011114	
			US 2002-53507 A220020117	

AB Optophoretic methods are used to determine one or more biol. properties or changes in biol. properties of one or more cells or cellular components. The methods use optical or photonic forces to select, identify, characterize, and/or sort whole cells or groups of cells. The methods are useful in a number of applications, including, but not limited to, drug screening applications, toxicity applications, protein expression applications, rapid clonal selection applications, biopharmaceutical monitoring and quality control applications, cell enrichment applications, viral detection, bacterial drug sensitivity screening, environmental testing, agricultural testing, food safety testing, as well as biohazard detection and anal. A whole blood sample was stained for 15 min with New Methylene Blue, a nucleic acid stain that differentially stains the nucleated white blood cells vs. the unnucleated red blood cells. The sample was diluted in PBS and mounted on a fluorosilane coated slide. A Michelson interferometer and a 150 mW, 812 nm laser system was used to generate optical gradient fields. The fringe period was adjusted to 15 μm and was moved at 22 μm/s. The white blood cells were moved by the fringes while the red blood cells were not.

IT **220127-57-1**, Gleevec
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cells response to; apparatus and method for optical interrogation to determine
biol. properties of cells or population of cells)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA

INDEX NAME)

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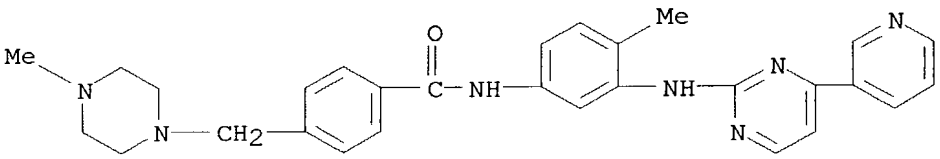
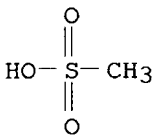
CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 49 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:483832 CAPLUS
DN 139:207284
TI SU11248 inhibits KIT and **platelet**-derived growth factor receptor β in preclinical models of human small cell lung cancer
AU Abrams, Tinya J.; Lee, Leslie B.; Murray, Lesley J.; Pryer, Nancy K.; Cherrington, Julie M.
CS Preclinical Research and Exploratory Development, Sugen, Inc., South San Francisco, CA, 94080, USA
SO Molecular Cancer Therapeutics (2003), 2(5), 471-478
CODEN: MCTOCF; ISSN: 1535-7163
PB American Association for Cancer Research
DT Journal
LA English
AB The purpose of this study was to evaluate the activity of the indolinone kinase inhibitor SU11248 against the receptor tyrosine kinase KIT in vitro and in vivo, examine the role of KIT in small cell lung cancer (SCLC), and anticipate clin. utility of SU11248 in SCLC. SU11248 is an oral, multitargeted tyrosine kinase inhibitor with direct antitumor and antiangiogenic activity through targeting **platelet**-derived growth factor receptor (PDGFR), vascular endothelial growth factor receptor, KIT, and FLT3 receptors. Treatment of the KIT-expressing SCLC-derived NCI-H526 cell line in vitro with SU11248 resulted in dose-dependent inhibition of stem cell factor-stimulated KIT phosphotyrosine levels and proliferation. The biol. significance of KIT inhibition was evaluated in vivo by treating mice bearing s.c. NCI-H526 tumors with SU11248 or another structurally unrelated KIT inhibitor, STI571 (Gleevec), which is also known to inhibit Bcr-AbI and PDGFRβ.

SU11248 treatment resulted in significant tumor growth inhibition, whereas inhibition from STI571 treatment was less dramatic. Both compds. reduced phospho-KIT levels in NCI-H526 tumors, with a greater reduction by SU11248, correlating with efficacy. Likewise, phospho-PDGFRβ levels contributed by tumor stroma and with known involvement in angiogenesis were strongly inhibited by SU11248 and less so by STI571. Because platinum-based chemotherapy is part of the standard of care for SCLC, SU11248 was combined with cisplatin, and significant tumor growth delay was measured compared with either agent alone. These results expand the profile of SU11248 as a KIT signaling inhibitor and suggest that SU11248 may have clin. potential in the treatment of SCLC via direct antitumor activity mediated via KIT as well as tumor angiogenesis via vascular endothelial growth factor receptor FLK1/KDR and PDGFRβ.

IT **220127-57-1**, Gleevec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SU11248 inhibits KIT and **platelet**-derived growth factor receptor β in preclin. models of human small cell lung cancer)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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CRN 152459-95-5
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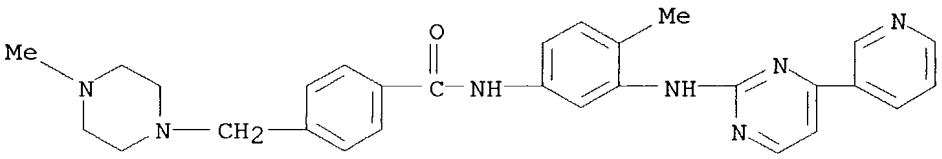
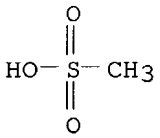


CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 50 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:471817 CAPLUS
DN 139:159626
TI Results of imatinib mesylate therapy in patients with refractory or recurrent acute myeloid leukemia, high-risk myelodysplastic syndrome, and

myeloproliferative disorders

AU Cortes, Jorge; Giles, Francis; O'Brien, Susan; Thomas, Deborah; Albitar, Maher; Rios, Mary Beth; Talpaz, Moshe; Garcia-Manero, Guillermo; Faderl, Stefan; Letvak, Laurie; Salvado, August; Kantarjian, Hagop

CS Department of Leukemia, M. D. Anderson Cancer Center, The University of Texas, Houston, TX, USA

SO Cancer (New York, NY, United States) (2003), 97(11), 2760-2766
CODEN: CANCAR; ISSN: 0008-543X

PB John Wiley & Sons, Inc.

DT Journal

LA English

AB Imatinib mesylate is a selective tyrosine kinase inhibitor of c-abl, bcr/abl, c-kit, and **platelet**-derived growth factor-receptor (PDGF-R). C-kit is expressed in most patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) and PDGF has been implicated in the pathogenesis of myeloproliferative disorders (MPD). The authors investigated the efficacy of imatinib in patients with these disorders. Forty-eight patients with AMI, (n = 10), MDS (n = 8), myelofibrosis (n = 18), atypical chronic myeloid leukemia (CML; n = 7), chronic myelomonocytic leukemia (CMML; n = 3), or polycythemia vera (n = 2) were treated with imatinib 400 mg daily. None of the patients with AML or MDS responded. Among patients with myelofibrosis, 10 of 14 patients with splenomegaly (71%) had a 30% or greater reduction in spleen size, 1 patient had trilineage hematol. improvement, 2 had erythroid hematol. improvement, and 1 had improvement in **platelet** count. One patient with atypical CML had erythroid hematol. improvement. Both patients with polycythemia vera needed fewer phlebotomies (from 2-3 per yr to none during the 8 mo of therapy and from 3-6 per yr to 1 during 9 mo of therapy). None of the three patients with CMML responded. Treatment was well tolerated. The side effects were similar to those observed in patients with CML. Within these small subgroups of disease types, single-agent imatinib did not achieve a significant clin. response among patients with AML, MDS, atypical CML, or CMML without PDGF-R fusion genes. Preliminary data on polycythemia vera are promising and deserve further investigation. Responses among myelofibrosis patients were minor. Therefore, a combination treatment regimen including imatinib may be more effective.

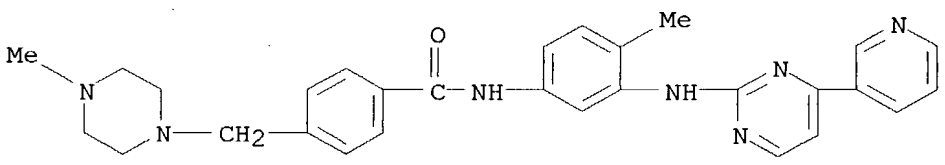
IT **220127-57-1**, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate in patients with acute myeloid leukemia, yelodysplastic syndrome and myeloproliferative disorders)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

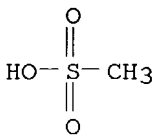
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 51 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:439253 CAPLUS
DN 139:131478
TI Philadelphia chromosome-positive leukemias: From basic mechanisms to molecular therapeutics
AU Kurzrock, Razelle; Kantarjian, Hagop M.; Druker, Brian J.; Talpaz, Moshe
CS Anderson Cancer Center, University of Texas M.D., Houston, TX, 77030, USA
SO Annals of Internal Medicine (2003), 138(10), 819-830
CODEN: AIMEAS; ISSN: 0003-4819
PB American College of Physicians-American Society of Internal Medicine
DT Journal; General Review
LA English
AB A review. The Philadelphia chromosome translocation (t(9;22)) results in the mol. juxtaposition of 2 genes, BCR and ABL, to form an aberrant BCR-ABL gene on chromosome 22. BCR-ABL is critical to the pathogenesis of chronic myelogenous leukemia and a subset of acute leukemias. The chimeric Bcr-Abl protein has constitutively elevated tyrosine phosphokinase activity. This abnormal enzymic activation is critical to the oncogenic potential of Bcr-Abl. Initially, protein kinases were thought to be poor therapeutic targets because of their ubiquitous nature and crucial role in many normal physiol. processes. However, the advent of imatinib mesylate (Gleevec, Novartis Pharmaceuticals, Basel, Switzerland), formerly known as ST1571 and CGP57148B, demonstrated that designer kinase inhibitors could be specific. This agent has shown striking activity in chronic myelogenous leukemia. It also inhibits phosphorylation of Kit (stem-cell factor receptor) and **platelet**-derived growth factor receptor. In addition, it has shown similar impressive responses, with little host toxicity, in gastrointestinal stromal tumors, which harbor activating Kit mutations, and in tumors with activated **platelet** -derived growth factor receptor. The studies of imatinib mesylate provide proof-of-principle for using aberrant kinases as a therapeutic target and are a model for the promise of mol. therapeutics. This paper reviews the current knowledge on the function of Bcr-Abl and its normal counterparts (Bcr and Abl), as well as the impact of this knowledge on the development of a remarkably successful targeted therapy approach.
IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. genetics and imatinib mesylate therapy of Philadelphia chromosome-pos. leukemias)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-

pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
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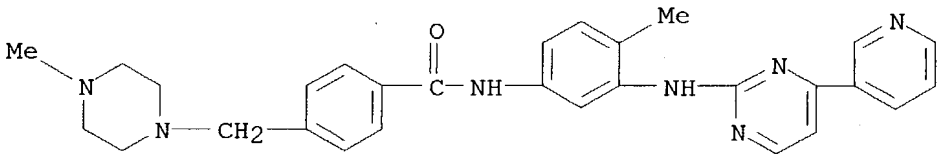

CM 2

CRN 75-75-2
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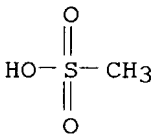

RE.CNT 124 THERE ARE 124 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 52 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:413877 CAPLUS
DN 138:396218
TI Combination for the treatment of endothelial damage
IN Alitalo, Kari; Heldin, Carl Henrik; Leppanen, Olli; Ostman, Arne; Yla-Herttuala, Seppo
PA Finland
SO U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003099687	A1	20030529	US 2002-227081	20020823
			GB 2001-20690 A	20010824

AB The invention relates to a combination of (a) an inhibitor of **platelet**-derived growth factor (PDGF) activity and (b) a vector for vascular endothelial growth factor (VEGF-, especially VEGF-C) gene transfer,
a pharmaceutical preparation comprising (a) and (b) in combination together with a pharmaceutically acceptable carrier material; a product comprising (a) and (b) as defined above and optionally a pharmaceutically acceptable carrier material, for simultaneous, chronol. staggered or sep. use; a method of administering or the use of said combination or product for the

treatment of endothelial damage; and/or to the use of (a) and (b) for the manufacture of said pharmaceutical preparation or product for the treatment of endothelial damage.

IT **220127-57-1**, STI571
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination for treatment of vascular endothelial damage using **platelet**-derived growth factor inhibitors and gene transfer of vascular endothelial growth factor in relation to formulation and pharmacokinetics)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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CRN 152459-95-5
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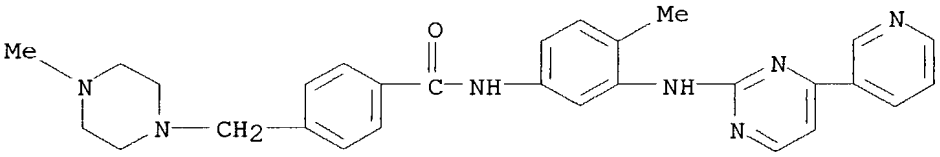

CM 2

CRN 75-75-2
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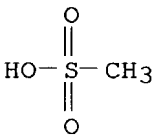

L17 ANSWER 53 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:362915 CAPLUS

DN 139:78858

TI Imatinib therapy for hypereosinophilic syndrome and other eosinophilic disorders

AU Pardanani, Animesh; Reeder, Terra; Porrata, Luis F.; Li, Chin-Yang; Tazelaar, Henry D.; Baxter, E. Joanna; Witzig, Thomas E.; Cross, Nicholas C. P.; Tefferi, Ayalew

CS Divisions of Hematology and Internal Medicine, Hematopathology, and Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, 55905, USA

SO Blood (2003), 101(9), 3391-3397
CODEN: BLOOAW; ISSN: 0006-4971

PB American Society of Hematology

DT Journal

LA English

AB Imatinib mesylate (Gleevec), a small mol. inhibitor of abl, kit, and **platelet**-derived growth factor receptor (PDGFR) tyrosine kinases, has been reported to be effective in the treatment of hypereosinophilic syndrome (HES) and a rare eosinophilia-associated chronic myeloid disorder (eos-CMD) characterized by the t(5;12)(q33;p13) cytogenetic abnormality. In the current study, we sought to confirm the preliminary observations in HES as well as evaluate the therapeutic value of imatinib in eos-CMD that is not associated with t(5;12)(q33;p13). Five patients with HES (all men, median age = 46 yr) and 2 with eos-CMD (both men, aged 45 and 58 yr) were treated with imatinib at a starting dose of 100 to 400 mg/day. Cytogenetic studies showed no evidence of either the bcr-abl translocation or t(5;12)(q33;p13) in any patient. Screening of exons encoding the intracellular catalytic domains and extra-cellular ligand binding domains of PDGFRβ (exons 2-23) and c-kit (exons 1-21) in 6 patients demonstrated mostly previously known polymorphisms. At a median follow-up of 17 wk (range, 10-33 wk), 2 patients with HES and 1 with eos-CMD have achieved complete clin. remission and 1 addnl. patient with HES has achieved a partial remission. In contrast to previous observations, all 4 responding patients had elevated serum interleukin-5 levels. Although the drug was well tolerated in most patients, a previously unrecognized treatment toxicity of acute left ventricular dysfunction occurred in a responding patient with HES within the first week of treatment. Myocardial biopsy revealed eosinophilic infiltration and degranulation, and the cardiogenic shock was reversed with the prompt institution of corticosteroid therapy.

IT **220127-57-1**, Gleevec
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate (Gleevec) for hypereosinophilic syndrome and other eosinophilic disorders)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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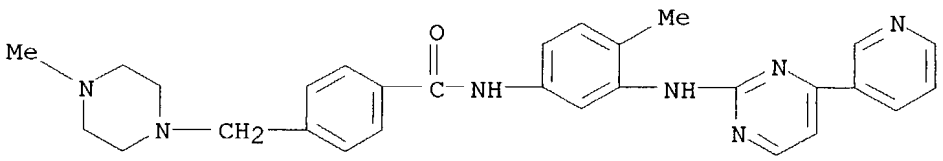

CM 2

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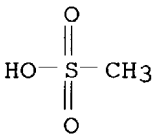

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 54 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:337290 CAPLUS
DN 139:66903
TI Genetics of dermatofibrosarcoma protuberans family of tumors: From ring chromosomes to tyrosine kinase inhibitor treatment
AU Sirvent, Nicolas; Maire, Georges; Pedeutour, Florence
CS Service de Pediatrie, Centre hospitalier universitaire de Nice, Nice, Fr.
SO Genes, Chromosomes & Cancer (2003), 37(1), 1-19
CODEN: GCCAES; ISSN: 1045-2257
PB Wiley-Liss, Inc.
DT Journal; General Review
LA English
AB A review. Dermatofibrosarcoma protuberans (DP) is a rare, slow-growing, infiltrating dermal neoplasm of intermediate malignancy, made up of spindle-shaped tumor cells often pos. for CD34. The preferred treatment is wide surgical excision with pathol. neg. margins. At the cytogenetic level, DP cells are characterized by either supernumerary ring chromosomes, which have been shown by using fluorescence in situ hybridization techniques to be derived from chromosome 22 and to contain low-level amplified sequences from 17q22-qter and 22q10-q13.1, or t(17;22), that are most often unbalanced. Both the rings and linear der(22) contain a specific fusion of COL1A1 with PDGFB. Similar to other tumors, the COL1A1-PDGFB fusion is occasionally cryptic, associated with complex chromosomal rearrangements. Although rings have been mainly observed in adults, translocations have been reported in all pediatric cases. DP is therefore a unique example of a tumor in which (i) the same mol. event occurs either on rings or linear translocation derivs., (ii) the chromosomal abnormalities display an age-related pattern, and (iii) the presence of the specific fusion gene is associated with the gain of chromosomal segments, probably taking advantage of gene dosage effects. In all DP cases that underwent mol. investigations, the breakpoint localization in PDGFB was found to be remarkably constant, placing exon 2 under the control of the COL1A1 promoter. In contrast, the COL1A1 breakpoint was found to be variably located within the exons of the α-helical coding region (exons 6-49). No preferential COL1A1 breakpoint and no correlation between the breakpoint location and the age of the patient or any clin. or histol. particularity have been described. The COL1A1-PDGFB fusion is detectable by multiplex RT-PCR with a combination of forward primers designed from a variety of COL1A1 exons and one reverse primer from PDGFB exon 2. Recent studies have determined the mol. identity of "classical" DP, giant cell fibroblastoma, Bednar tumor, adult superficial fibrosarcoma, and the granular cell variant of DP. In approx. 8% of DP cases, the COL1A1-PDGFB fusion is not found, suggesting that genes other than COL1A1 or PDGFB might be involved in a subset of cases. It has been proposed that PDGFB acts as a mitogen in DP cells by autocrine stimulation of the PDGF receptor. It is encouraging that inhibitory effects of the PDGF receptor tyrosine kinase antagonist imatinib mesylate have been demonstrated in vivo; such targeted therapies might be warranted in the near future for treatment of the few DP cases not manageable by

surgery.

IT **220127-57-1**, Imatinib mesylate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(COL1A1-PDGFB gene fusion of dermatofibrosarcoma protuberans family of tumors involving ring chromosomes and tyrosine kinase inhibitor treatment)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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CRN 152459-95-5
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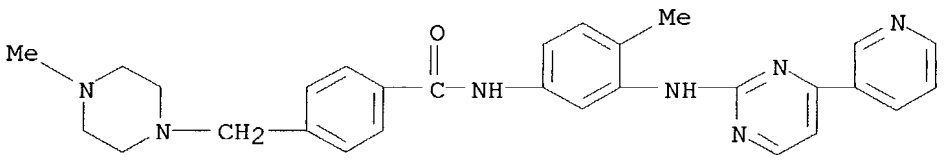
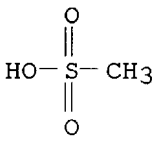


CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 110 THERE ARE 110 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 55 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:314937 CAPLUS
DN 139:46643
TI Sustained complete hematologic remission after administration of the tyrosine kinase inhibitor imatinib mesylate in a patient with refractory, secondary acute lymphoblastic leukemia
AU Kindler, Thomas; Breitenbuecher, Frank; Marx, Andreas; Hess, Georg; Gschaidmeier, Harald; Gamm, Heinold; Kirkpatrick, Charles J.; Huber, Christoph; Fischer, Thomas
CS Department of Hematology/Oncology, Johannes Gutenberg University, Mainz, 55101, Germany
SO Blood (2003), 101(8), 2960-2962
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Imatinib mesylate, a tyrosine kinase inhibitor targeting bcr-abl,

platelet-derived growth factor receptor (PDGF-R), and c-Kit, effectively induces hematol. and cytogenetic remissions in bcr-abl+ chronic myeloid leukemia (CML) and acute lymphoblastic leukemia (ALL) with only mild to moderate side effects. Here, we describe the successful treatment of a 64-yr-old man with c-Kit+ secondary acute myeloid leukemia (AML) refractory to standard chemotherapy. Upon 2 wk of imatinib mesylate administration, the patient achieved a complete hematol. remission in peripheral blood. In addition, complete clearance of leukemic blasts in bone marrow and a significant cytogenetic response lasting for more than 5 mo was observed Sequence anal. of exons 2, 8, 10, 11, and 17 of the c-Kit receptor did not reveal structural alterations as previously described in a subset of AML cases. This is the first report of complete remission achieved upon administration of imatinib mesylate in a patient with highly refractory, secondary AML.

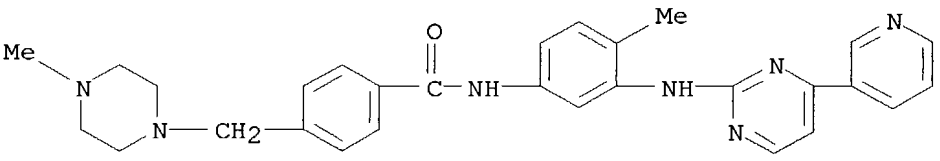
IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tyrosine kinase inhibitor imatinib mesylate in patient with acute lymphoblastic leukemia)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

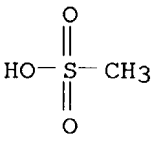
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



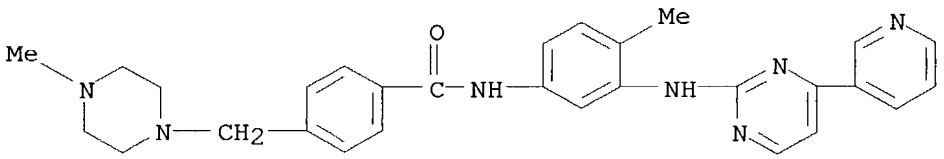
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 56 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:308889 CAPLUS
DN 139:46642
TI Imatinib mesylate: in the treatment of gastrointestinal stromal tumors

AU Croom, Katherine F.; Perry, Caroline M.
CS Adis International Limited, Auckland, N. Z.
SO Drugs (2003), 63(5), 513-522
CODEN: DRUGAY; ISSN: 0012-6667
PB Adis International Ltd.
DT Journal
LA English
AB Imatinib mesylate (imatinib) is an orally administered competitive inhibitor of the tyrosine kinases associated with the KIT protein (stem cell factor receptor), ABL protein and **platelet**-derived growth factor receptors. The KIT tyrosine kinase is abnormally expressed in gastrointestinal stromal tumor (GIST), a rare neoplasm for which there has been no effective systemic therapy. In a randomized, nonblind, multicenter study that evaluated imatinib 400 or 600mg once daily in 147 patients with advanced GIST, confirmed partial responses were achieved in 54% of patients overall (median duration of follow-up was 288 days). Stable disease was experienced by 28% of patients and the estimated 1-yr survival rate was 88%. Similar response rates were reported in a smaller, dose-escalation study, in which objective tumor response was a secondary endpoint. Although nearly all patients with GIST treated with imatinib experienced adverse events, most events were mild or moderate in nature. Severe or serious adverse events occurred in 21% of patients in the larger study, and included gastrointestinal or tumor hemorrhage.
IT **220127-57-1**, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate in treatment of gastrointestinal stromal tumors)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

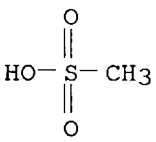
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

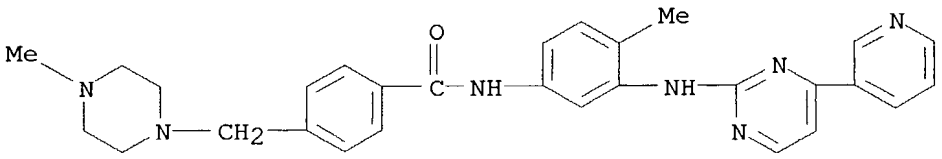


RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 57 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:277575 CAPLUS
DN 139:47492
TI Inhibition of protein kinase C decreases prostaglandin-induced breakdown of the blood-retinal barrier
AU Saishin, Yoshitsugu; Saishin, Yumiko; Takahashi, Kyoichi; Melia, Michele; Vinores, Stanley A.; Campochiaro, Peter A.
CS The Departments of Ophthalmology and Neuroscience, The Johns Hopkins University School of Medicine, Baltimore, MD, 21287-9277, USA
SO Journal of Cellular Physiology (2003), 195(2), 210-219
CODEN: JCLLAX; ISSN: 0021-9541
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Breakdown of the blood-retinal barrier (BRB) occurs in several retinal diseases and is a major cause of visual loss. Vascular endothelial growth factor (VEGF) has been implicated as a cause of BRB breakdown in diabetic retinopathy and other ischemic retinopathies, and there is evidence to suggest that other vasopermeability factors may act indirectly through VEGF. In this study, we investigated the effect of several receptor kinase inhibitors on BRB breakdown resulting from VEGF, tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), insulin-like growth factor-1 (IGF-1), prostaglandin E1 (PGE1), or PGE2. Inhibitors of VEGF receptor kinase, including PKC412, PTK787, and SU1498, decreased VEGF-induced breakdown of the BRB. None of the inhibitors blocked leakage caused by TNF-α, IL-1β, or IGF-1 and only PKC412, an inhibitor of protein kinase C (PKC) as well as VEGF and **platelet**-derived growth factor (PDGF) receptor kinases, decreased leakage caused by prostaglandins. Since the other inhibitors of VEGF and/or PDGF receptor kinases that do not also inhibit PKC had no effect on prostaglandin-induced breakdown of the BRB, these data implicate PKC in retinal vascular leakage caused by prostaglandins. PKC412 may be useful for treatment of post-operative and inflammatory macular edema, in which prostaglandins play a role, as well as macular edema associated with ischemic retinopathies.
T **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of protein kinase inhibitors on vasopermeability factors-induced breakdown of blood-retinal barrier)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

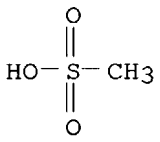
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 58 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:273871 CAPLUS
DN 139:66972
TI Expression of molecular targets for tyrosine kinase receptor antagonists in malignant endocrine pancreatic tumors
AU Fjaellskog, Marie-Louise H.; Lejonklou, Margareta H.; Oeberg, Kjell E.; Eriksson, Barbro K.; Janson, Eva T.
CS Department of Medical Sciences, University Hospital, Uppsala, SE-751 85, Swed.
SO Clinical Cancer Research (2003), 9(4), 1469-1473
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB Mol. targeting with monoclonal antibodies and tyrosine kinase inhibitors is a novel approach to cancer treatment. We have examined the expression of mol. targets in patients with malignant endocrine pancreatic tumors, which is necessary to justify addnl. studies investigating the potential benefit from such treatment. Thirty-eight tumor tissues from malignant endocrine pancreatic tumors were examined with immunohistochem. using specific polyclonal antibodies with regard to the expression pattern of **platelet**-derived growth factor receptors (PDGFRs) α and β, c-kit, and epidermal growth factor receptor (EGFR). All 38 tissue specimens expressed PDGFRα on tumor cells, and 21 of 37 specimens (57%) expressed PDGFRα in tumor stroma (1 specimen was nonevaluable). Twenty-eight samples (74%) stained pos. for PDGFRβ on tumor cells, and 36 of 37 samples (97%) stained pos. for PDGFRβ in the stroma (1 specimen was nonevaluable). Thirty-five tumor tissues (92%) stained pos. for c-kit, and 21 (55%) stained pos. for EGFR on tumor cells. No differences were seen between syndromes or between poorly differentiated or well-differentiated tumors. Previous treatment did not influence expression pattern. Receptor expression pattern varied considerably between individuals. We have found that tyrosine kinase receptors PDGFRs α and β, EGFR, and c-kit are expressed in more

than half of the patients with endocrine pancreatic tumors. Because these receptors represent mol. targets for STI571 and ZD1839 (tyrosine kinase inhibitors) and IMC-C225 (a monoclonal antibody), we propose that patients suffering from EPTs might benefit from this new treatment strategy. However, because of great variability in receptor expression pattern, all patients' individual receptor expression should be examined

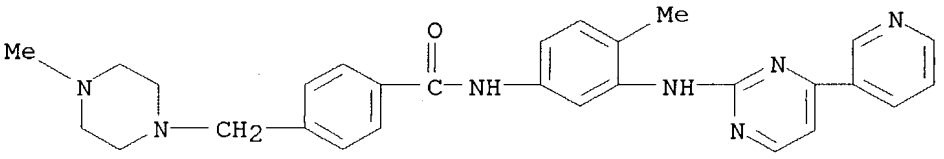
IT **220127-57-1,** STI571
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(expression of mol. targets for tyrosine kinase receptor antagonists in malignant endocrine pancreatic tumors)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

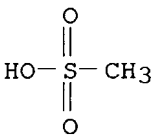
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 59 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:273838 CAPLUS
DN 139:345024
TI Is Another Bcr-Abl Inhibitor Needed for Chronic Myelogenous Leukemia?
AU Sausville, Edward A.
CS Developmental Therapeutics Program, National Cancer Institute, Rockville, MD, 20852, USA
SO Clinical Cancer Research (2003), 9(4), 1233-1234
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal; General Review
LA English
AB A review. The recent success of STI-571 (imatinib mesylate; Gleevec) in

the chronic phase of chronic myelogenous leukemia (CML) is a milestone in the history of medicine. For the first time, a treatment directed at the mol. basis for a tumor's occurrence and progression has emerged. Such molecularly-targeted agents are the focus of current developmental research, with hoped for applications across a broad range of potential targets and tumors. In this issue is a report that the pyridopyrimidine PD166326, representative of a new chemical class, possesses picomolar potency against p210bcr/abl kinase in biochem. assays and nanomolar potency against p210bcr/ab-driven cell lines, both assayed in vitro, but more potent than STI-571 with respect to these endpoints. Given the success of STI-571, however, it is reasonable to question whether there is need and practical value in further pursuing the development of this compound, especially given the limited number of patients afflicted with CML. The immediate and unflinching answer to this question is a resounding yes!. Multiple reasons support this position. STI-571 is an ATP-binding site directed inhibitor with selective activity against the abl, kit, and **platelet**-derived growth factor receptor kinases. Accordingly, it has shown gratifying activity not only in chronic phase CML but also in kit-driven gastrointestinal stromal tumors and shows promise in **platelet**-derived growth factor receptor-driven proliferations such as dermatofibrosarcoma protuberans. However, it is not by any means a perfect drug. Patients with blast phase CML show more limited or essentially no response to STI-571. Multiple mechanisms of resistance are emerging to STI-571, including p210bcr/abl gene amplification, mutations, and host-related elaboration of α1-acid glycoprotein. Thus, one can hardly maintain that the book should be closed on developing bcr-abl-directed therapies.

IT **220127-57-1**, STI-571
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison; antitumor activity of Bcr-Abl inhibitor PD166326 in chronic myelogenous leukemia)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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CRN 152459-95-5
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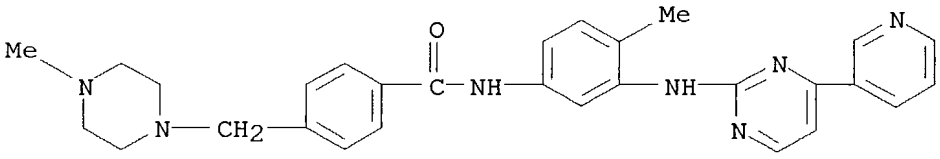
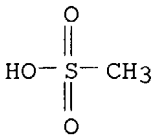


CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 60 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:273837 CAPLUS
DN 139:345023
TI Molecular Therapeutics: Is One Promiscuous Drug against Multiple Targets Better than Combinations of Molecule-specific Drugs?
AU Arteaga, Carlos L.
CS Vanderbilt-Ingram Comprehensive Cancer Center, Departments of Medicine and Cancer Biology, and Breast Cancer Program, Vanderbilt University School of Medicine, Nashville, TN, 37232, USA
SO Clinical Cancer Research (2003), 9(4), 1231-1232
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal; General Review
LA English
AB A review, discussing the benefits and disadvantages of two different approaches to mol.-targeted therapeutics, i.e., the use of promiscuous small mol. inhibitors acting against multiple targets, such as ZD6474, SU6668, or STI-571, vs. combinations of inhibitors, such as ZD1839, SC-236, and antisense oligonucleotide against protein kinase A type I that work together in an additive or synergistic way.
IT **220127-57-1**, STI-571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benefits and disadvantages of two approaches to mol. therapeutics comparing promiscuous drugs against multiple targets with combinations of mol.-specific drugs)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
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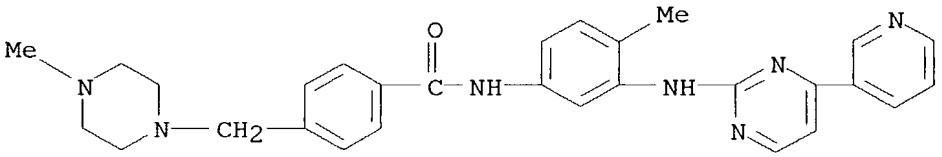

CM 2

CRN 75-75-2

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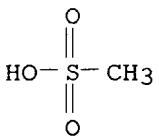

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 61 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:254912 CAPLUS
DN 139:316760
TI Effects of Blocking **Platelet**-Derived Growth Factor-Receptor Signaling in a Mouse Model of Experimental Prostate Cancer Bone Metastases
AU Uehara, Hisanori; Kim, Sun Jin; Karashima, Takashi; Shepherd, David L.; Fan, Dominic; Tsan, Rachel; Killion, Jerald J.; Logothetis, Christopher; Mathew, Paul; Fidler, Isaiah J.
CS Dep. of Cancer Biol., The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SO Journal of the National Cancer Institute (2003), 95(6), 458-470
CODEN: JNCIEQ; ISSN: 0027-8874
PB Oxford University Press
DT Journal
LA English
AB Expression of **platelet**-derived growth factor (PDGF) and activation (by autophosphorylation) of its receptor (PDGF-R), a tyrosine kinase, are associated with the growth of metastatic prostate tumor cells in the bone parenchyma. The tyrosine kinase inhibitor STI571 blocks the PDGF signaling pathway by inhibiting PDGF-R autophosphorylation. We examined the effects of STI571, given alone or with paclitaxel (Taxol), on tumor growth in a mouse model of prostate cancer metastasis. Human prostate cancer PC-3MM2 cells were injected into the tibias of male nude mice. Three days later the mice (20 per group) were randomly assigned to 5 wk of treatment with oral and injected water (control), daily oral STI571, weekly injected paclitaxel, or STI571 plus paclitaxel. Lesions in bone and the surrounding muscles were then harvested and analyzed by histol., western blotting (for PDGF-R phosphorylation), immunohistochem. (for expression of pro-angiogenic mols.), and double immunofluorescence (to identify endothelial cells and apoptotic tumor cells). Growth of bone lesions was monitored by digital radiog. Bone lesions from control mice were used to establish short-term cell cultures for anal. of PDGF-R phosphorylation. All statistical tests were two-sided. PC-3MM2 cells cultured from bone lesions and treated in vitro with STI571 had less phosphorylated PDGF-R than untreated cells. In control mice, bone lesions expressed high levels of PDGF and activated (i.e., phosphorylated) PDGF-R, whereas lesions in the adjacent musculature did not. Activated PDGF-R was present on the surface of endothelial cells within the bone lesions but not in endothelial cells of uninjected bone. Mice treated with STI571 or STI571 plus paclitaxel had a lower tumor incidence, smaller tumors, and less bone lysis and lymph node metastasis than mice treated with water or paclitaxel alone ($P<.001$ for all). Mice treated with STI571 or STI571 plus paclitaxel had less phosphorylated PDGF-R on tumor cells and tumor-associated endothelial cells, less tumor cell proliferation, statistically significantly more apoptotic tumor cells (all $P<.001$), and fewer tumor-associated endothelial cells ($P<.001$) than control mice. Endothelial

cells appear to express phosphorylated PDGF-R when they are exposed to tumor cells that express PDGF. Using STI571 to inhibit PDGF-R phosphorylation may, especially in combination with paclitaxel, produce substantial therapeutic effects against prostate cancer bone metastasis.

IT **220127-57-1**, STI571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of blocking **platelet**-derived growth factor-receptor signaling in mouse model of exptl. prostate cancer bone metastases)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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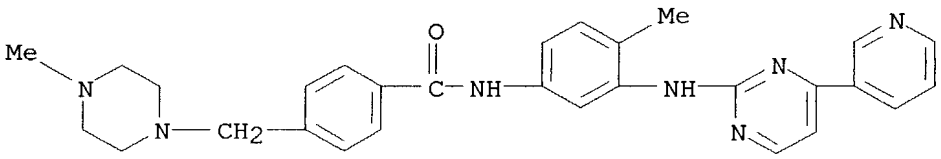
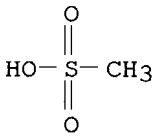
CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 62 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:126182 CAPLUS
DN 139:270629
TI **Platelet**-derived growth factor receptor inhibition reduces allograft arteriosclerosis of **heart** and aorta in cholesterol-fed rabbits
AU Sihvola, Roope K.; Tikkanen, Jussi M.; Krebs, Rainer; Aaltola, Eva M.; Buchdunger, Elisabeth; Laitinen, Outi; Koskinen, Petri K.; Lemstroem, Karl B.
CS Transplantation Laboratory, Cardiopulmonary Research Group, Univ. of Helsinki, Helsinki University Central Hosp., Helsinki, Finland
SO Transplantation (2003), 75(3), 334-339
CODEN: TRPLAU; ISSN: 0041-1337
PB Lippincott Williams & Wilkins

DT Journal
LA English
AB Crosstalk between pro-inflammatory cytokines and **platelet**-derived growth factor (PDGF) regulates smooth-muscle-cell proliferation in **cardiac**-allograft arteriosclerosis. In this study, we tested the effect of STI 571, a novel orally active protein tyrosine kinase (PTK) inhibitor selective for PDGF receptor (PDGF-R) on transplant and accelerated arteriosclerosis in hypercholesterolemic rabbits. **Cardiac** allografts were transplanted heterotopically from Dutch Belted to New Zealand White rabbits. A 0.5% cholesterol diet was begun 4 days before transplantation. Recipients received STI 571 5 mg/kg per day or vehicle i.p. throughout the study period of 6 wk. Cyclosporine A was given as background immunosuppression. In **cardiac** allografts of vehicle-treated rabbits, 76.2±2.1% of medium-sized **arteries** were affected by intimal thickening, and the percentage of arterial occlusion was 45.0±5.0%. Treatment with STI 571 reduced the incidence of affected medium-sized **arteries** to 41.2±8.1% (<0.05) and the arterial occlusion to 27.6±5.0% (<0.05). In addition, we observed that STI 571 treatment reduced intimal lesion formation in proximal ascending aorta of transplanted hearts from 72.3±19.9 to 12.7±1.9 μm (<0.05). Our results also show that STI 571 significantly inhibited accelerated arteriosclerosis in medium-sized **arteries** of recipients' own hearts. The results of the present study suggest that PDGF-R activation may regulate the development of transplant and accelerated arteriosclerosis in hypercholesterolemic rabbits. Thus, PTK inhibitors may provide new strategies for prevention of these fibroproliferative vascular disorders.
IT **220127-57-1**, STI 571
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PDGFR inhibition reduces allograft arteriosclerosis of **heart** and aorta in cholesterol-fed rabbits)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
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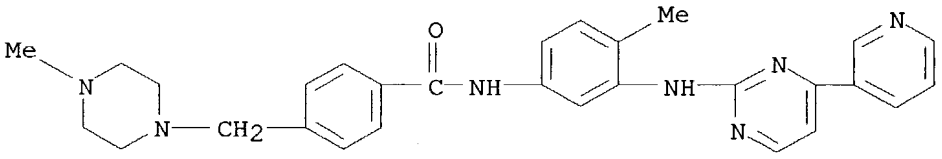
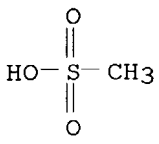


CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 63 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:117782 CAPLUS
DN 138:153689
TI Preparation of retinoid derivatives with antiangiogenic, antitumoral and proapoptotic activities
IN Merlini, Lucio; Dallavalle, Sabrina; Penco, Sergio; Giannini, Giuseppe; Pisano, Claudio; Vesci, Loredana
PA Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., Italy
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

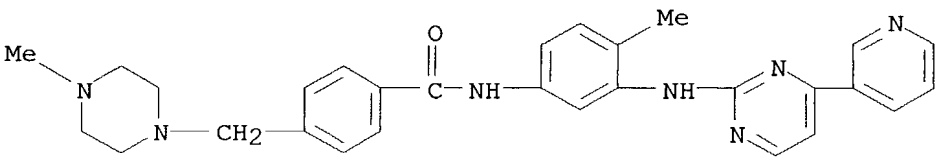
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003011808	A1	20030213	WO 2002-IT474	20020718
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			IT 2001-RM464	A 20010731
EP 1412317	A1	20040428	EP 2002-760553	20020718
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
			IT 2001-RM464	A 20010731
			WO 2002-IT474	W 20020718

OS MARPAT 138:153689
AB Retinoid derivs., such as I [R1 = alkyl, cycloalkyl, heterocycloalkyl, (un)substituted Ph, adamantyl; R2 = OR5, OCOR5, CO2R5; R3 = H, OH, O-alkyl, (CH2)n-NH2, (CH2)n-NH-alkyl, (CH2)n-OH, where n = 1-4; R4 = tetrazole, SO3H, NHSO3H, CHO, CO2H, CO2-alkyl, CONHOH, CONH-aryl, PO3H2; R5 = H, alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, SO3H; A = [C(R6,R7)-C(R8,R9)]m, [C(R10):C(R11)]m, [C.tplbond.C]m; m = 0-3; R6, R7, R8, R9 = H, alkyl, halogen, OH, OR5, NO2, NH2, aryl; R10, R11 = H, OH, halogen, alkyl, aryl, CN, NO2, CO2R5], were prepared as useful agents in the cure of pathologies characterized by altered angiogenesis and as antitumorals. Thus, reaction between 2-(1-adamantyl)4-(4-bromophenyl)phenol and Me acrylate in presence of palladium acetate and tri-(o-tolyl)-phosphine provided retinoid derivative II (R = Me) which was hydrolyzed with lithium hydroxide monohydrate to afford II [R = H (III)]. III exhibited IC50 = 0.02 μM against promyelocytic leukemia NB4 cell line.

IT **220127-57-1**, Glivec
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of retinoid derivs. with antiangiogenic, antitumoral and proapoptotic activities)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

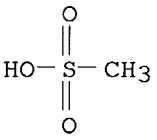
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 64 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:106984 CAPLUS
DN 138:214772
TI Preclinical and clinical profile of imatinib mesilate, a potent protein-tyrosine kinase inhibitor for CML therapy
AU Toga, Wakako; Kondo, Midori; Tokoro, Akio
CS Preclin. Dev. Div., Tsukuba Res. Inst., Novartis Pharma K. K., Tsukuba, 300-2611, Japan
SO Nippon Yakurigaku Zasshi (2003), 121(2), 119-128
CODEN: NYKZAU; ISSN: 0015-5691
PB Nippon Yakuri Gakkai
DT Journal; General Review
LA Japanese
AB A review. Imatinib mesilate (Glivec) is a protein-tyrosine kinase inhibitor that potently inhibits the Bcr-Abl tyrosine kinase as well as the receptors for **platelet**-derived growth factor (PDGF) and stem cell factor (SCF), c-Kit, at in vitro and cellular kinase assay levels. Since Bcr-Abl tyrosine kinase plays a key role in chronic myelogenous leukemia (CML) patients, treatment with imatinib mesilate that potently

inhibits Bcr-Abl tyrosine kinase could be a promising therapeutic approach to CML. Imatinib mesilate was shown to inhibit proliferation of bcr-abl-pos. cell lines and suppress the formation of bcr-abl-pos. colonies in cells derived from bone marrow of CML patients. This compound induced apoptosis in a variety of bcr-abl-pos. cells. Moreover, in vivo data indicated that imatinib mesilate suppress growth and formation of bcr-abl-pos. tumors in mice. As the profile expected from the preclin. studies, imatinib mesilate showed impressive hematol. and cytogenic responses in the clin. trials, including interferon-alpha-resistant or intolerant patients.

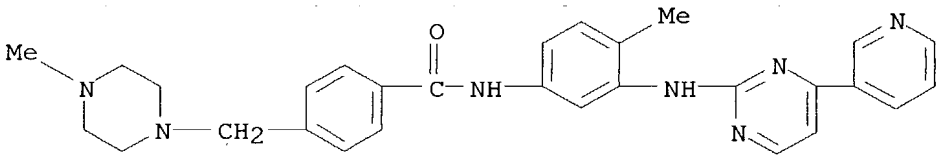
IT **220127-57-1**, Glivec
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preclin. and clin. profile of imatinib mesilate, potent protein-tyrosine kinase inhibitor for CML therapy)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

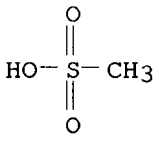
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

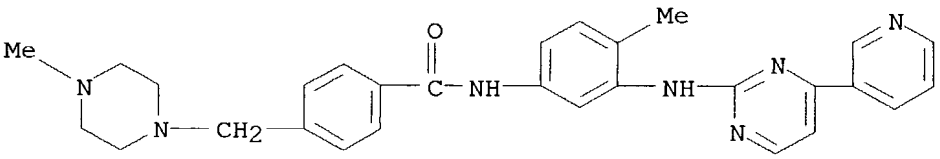


L17 ANSWER 65 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:106662 CAPLUS
DN 138:364636
TI A Single Amino Acid Exchange Inverts Susceptibility of Related Receptor Tyrosine Kinases for the ATP Site Inhibitor STI-571
AU Boehmer, Frank D.; Karagyozov, Luchezar; Uecker, Andrea; Serve, Hubert; Botzki, Alexander; Mahboobi, Siavosh; Dove, Stefan
CS Medical Faculty, Research Unit Molecular Cell Biology, Friedrich Schiller University, Jena, D-07747, Germany

SO Journal of Biological Chemistry (2003), 278(7), 5148-5155
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB The tyrosine kinase inhibitor STI-571 potently blocks BCR-Abl, **platelet**-derived growth factor (PDGF) α- and β-receptors, and c-Kit kinase activity. However Flt3, a receptor tyrosine kinase closely related to PDGF receptors and c-Kit, is not inhibited by STI-571. Sequence alignments of different kinases and indications from the crystal structure of the STI-571 Abl kinase complex revealed amino acid residues that are probably crucial for this activity profile. It was predicted that Flt3 Phe-691 in the β5 strand may sterically prevent interaction with STI-571. The point mutants Flt3 F691T and PDGFβ-receptor T681F were constructed, and kinase assays showed that the Flt3 mutant but not the PDGFβ-receptor mutant is inhibited by STI-571. Docking of STI-571 into computer models of the PDGFβ-receptor and Flt3 kinase domains and comparison with the crystal structure of the STI-571 Abl kinase complex indicated very similar binding sites among the three nonphosphorylated kinases, suggesting corresponding courses of their Asp-Phe-Gly motifs and activation loops. Accordingly, we observed reduced sensitivity of preactivated compared with nonactivated PDGFR-β for the inhibition by STI-571. Courses of the activation loop that collide with STI-571 binding explain its inactivity toward other kinases such as the insulin receptor. The binding site models of PDGFR-β and Flt3 were applied to predict structural approaches for more selective PDGFβ-receptor inhibitors.
IT **220127-57-1**, STI-571
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(single Phe-Thr exchange inverts susceptibility of related receptor tyrosine kinases Flt3 and PDGFβ-receptor toward ATP site inhibitor STI-571)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

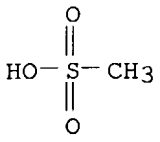
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

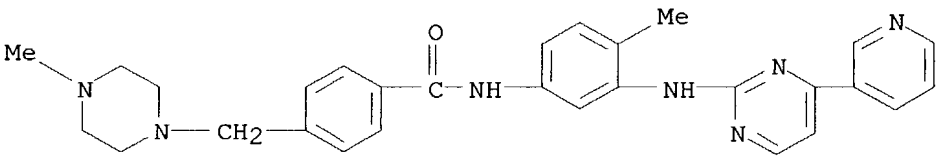


RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 66 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:13818 CAPLUS
DN 138:32998
TI Spontaneous reversion from blast to chronic phase after withdrawal of imatinib mesylate in a patient with chronic myelogenous leukemia
AU Liu, Nina Shih; O'Brien, Susan
CS Department of Leukemia, M.D. Anderson Cancer Center, The University of Texas, Houston, TX, 77030, USA
SO Leukemia & Lymphoma (2002), 43(12), 2413-2415
CODEN: LELYEA; ISSN: 1042-8194
PB Taylor & Francis Ltd.
DT Journal
LA English
AB Imatinib mesylate, a specific inhibitor of the BCR-ABL tyrosine kinase, has been very effective in the treatment of chronic myeloid leukemia (CML) in chronic phase with high rates of hematol. and cytogenetic remissions. Resistance to therapy can develop and transformation to blast crisis may occur, particularly in patients without a cytogenetic response. We report a case of a patient with CML treated in chronic phase who developed blast crisis; withdrawal of imatinib mesylate resulted in spontaneous reversion to chronic phase.
IT **220127-57-1**, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spontaneous reversion from blast to chronic phase after withdrawal of imatinib mesylate in patient with chronic myelogenous leukemia)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

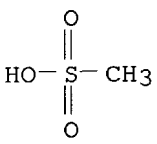
CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2

CMF C H4 O3 S



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 67 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:977959 CAPLUS
DN 138:51923
TI Mutations in the Bcr-Abl tyrosine kinase associated with resistance to STI-571
IN Sawyers, Charles L.; Gorre, Mercedes E.; Shah, Neil Pravin; Nicoll, John
PA The Regents of the University of California, USA
SO PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002102976	A2	20021227	WO 2002-US18729	20020614
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			US 2001-298728PP	20010614
			US 2001-331709PP	20011120
US 2003158105	A1	20030821	US 2002-171889	20020614
			US 2001-298728PP	20010614
			US 2001-331709PP	20011120

AB The invention described herein relates to novel genes and their encoded proteins, termed mutants associated with resistance to STI-571 (MARS) (e.g.,T315I Bcr-Abl), and to diagnostic and therapeutic methods and compns. useful in the management of various cancers that express MARS. STI-571 is only transiently effective in blast crisis and drug resistance emerges by amplification of or development of mutational changes in Bcr-Abl. A large scale sequencing project was carried out to identify mutations in the Abl kinase domain in patients with chronic myeloid leukemia using PCR to amplify a region of the Bcr-Abl transcript using primers specific to BCR and ABL. Over 40 point mutations are identified from patients with STI-571-resistant chronic myeloid leukemia. The invention further provides methods for identifying mols. that bind to and/or modulate the functional activity of MARS. Screening a family of Bcr-Abl tyrosine kinase inhibitors of the pyrido[2,3-d]pyrimidine class, unrelated to STI-571, identified a compound, PD166326, with substantial activity against STI-resistant mutant Bcr-Abl proteins.
IT **220127-57-1**, STI-571

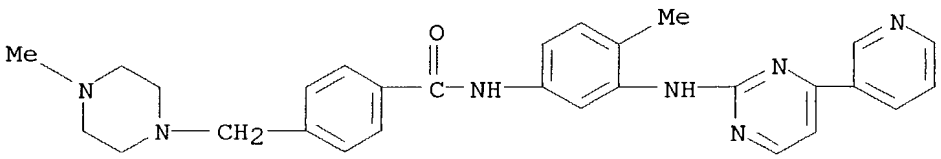
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mutations in the Bcr-Abl tyrosine kinase associated with resistance to STI-571)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

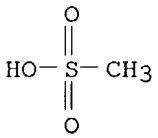
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 68 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:950177 CAPLUS

DN 138:32972

TI Response of extraabdominal desmoid tumors to therapy with imatinib mesylate

AU Mace, Joseph; Biermann, J. Sybil; Sondak, Vernon; McGinn, Cornelius; Hayes, Curtis; Thomas, Dafydd; Baker, Laurence

CS Division of Medical Oncology, Department of Internal Medicine, University of Michigan Medical Center, Ann Arbor, MI, USA

SO Cancer (New York, NY, United States) (2002), 95(11), 2373-2379
CODEN: CANCAR; ISSN: 0008-543X

PB John Wiley & Sons, Inc.

DT Journal

LA English

AB BACKGROUND: Desmoid tumor represents a rare monoclonal neoplasm arising from deep musculoaponeurotic structures and may occur sporadically or in association with the familial adenomatous polyposis and Gardner syndromes. Desmoid tumors do not appear to demonstrate metastatic potential; however, local infiltrative growth results in significant morbidity and potential mortality. Although the delineation of optimal therapy for desmoid tumors has been confounded by several factors, surgical resection with adjuvant

radiotherapy for a pos. surgical margin remains the standard approach. Responses have been demonstrated to nonsteroidal antiinflammatory agents, antiestrogen compds., and a variety of other agents in small series. Imatinib mesylate appears to demonstrate inhibitory activity against multiple class 3 receptor tyrosine kinases, including **platelet**-derived growth factor receptor (PDGFR)-α and PDGFR-β, as well as c-kit. METHODS: The authors performed immunohistochem. and qual. real-time polymerase chain reaction anal. on nine desmoid tumor specimens that demonstrated consistent positivity for c-kit as well as PDGFR-α and PDGFR-β. At the time of last follow-up, 2 patients had received therapy with imatinib mesylate at a dose of 400 mg twice daily. RESULTS: Both patients demonstrated ongoing radiog. and clin. responses with a duration of 9 mo and 11 mo, resp. CONCLUSIONS: Imatinib mesylate has been reported to have activity against desmoid tumor, most likely because of c-kit and PDGFR receptor tyrosine kinase activity inhibition, and warrants further study. The relative novelty of this agent and the lack of long-term toxicity data should prompt its use only in the salvage setting in which established local and systemic approaches fail to control disease. In addition, the use of imatinib mesylate in the treatment of this neoplasm preferably should be in the context of a formal prospective clin. trial.

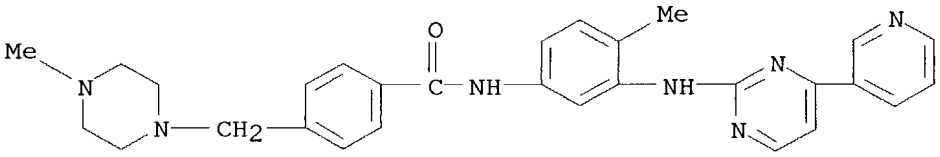
IT **220127-57-1,** Imatinib mesylate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(response to imatinib mesylate therapy in patients with extraabdominal desmoid tumors)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

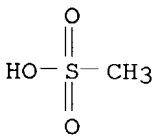
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 69 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:946113 CAPLUS
DN 138:24647
TI Preparation of 4-aryl-3-(3-aryl-1-oxo-2-propenyl)-2(1H)-quinolinones and analogs as activators of caspases and inducers of apoptosis for treatment of cancer and other proliferative disorders
IN Cai, Sui Xiong; Zhang, Han-Zhong; Drewe, John; Kasibhatla, Shailaja
PA Cytovia, Inc., USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

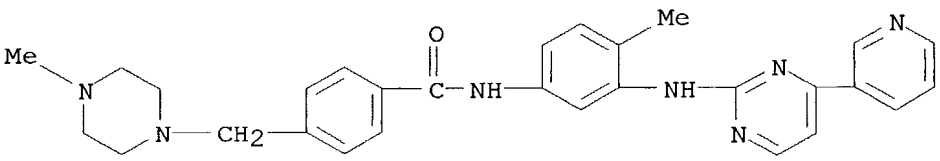
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002098425	A1	20021212	WO 2002-US17486	20020604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			US 2001-295007PP	20010604
EP 1404329	A1	20040407	EP 2002-741817	20020604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
			US 2001-295007PP	20010604
			WO 2002-US17486W	20020604

OS MARPAT 138:24647
AB Title compds. I [wherein R1-R4 = independently H, halo, (hetero)aryl, (halo)alkyl, (hetero)cycloalkyl, alkenyl, alkynyl, (hetero)arylalkyl, (hetero)arylalkenyl, hydroxyalkyl, NO2, NH2, CN, acylamino, OH, SH, acyloxy, azido, (halo)alkoxy, aryloxy, arylalkoxy, carboxy, carbonylamido, or alkylthio; R5, R6, and R12 = independently H or (un)substituted alkyl; Ar1 = (un)substituted (hetero)aryl, (partially) saturated carbocyclyl, or (partially) saturated heterocyclyl; Ar2 = (un)substituted (hetero)aryl; and pharmaceutically acceptable salts or prodrugs thereof] were prepared as activators of caspases and inducers of apoptosis. For example, 2-amino-2'-fluoro-5-bromobenzophenone was treated with diketene in pyridine to give 3-acetyl-6-bromo-4-(2-fluorophenyl)-2(1H)-quinolinone (89%). Condensation with m-nitrobenzaldehyde in EtOH produced the (3-nitrophenylpropenoyl)quinolinone II (R = NO2) in 42% yield. A related compound, II (R = H), activated caspase cascade activity with EC50 values of 849 nM and 1800 nM against human breast cancer cell lines T-47D and ZR-75-1, resp. Thus, I may be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs, such as cancer and other proliferative disorders.
IT **220127-57-1**, Gleevec
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration agent; coadministration of (arylpropenoyl)-2(1H)-quinolinone caspases activators with known cancer therapeutic agents for treatment of cancer)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

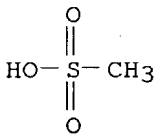
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 70 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:944375 CAPLUS
DN 139:78593
TI Inhibition of **platelet**-derived growth factor-mediated proliferation of osteosarcoma cells by the novel tyrosine kinase inhibitor STI571
AU McGary, Eric C.; Weber, Kristy; Mills, Lisa; Doucet, Michelle; Lewis, Valerie; Lev, Dina Chelouche; Fidler, Isaiah J.; Bar-Eli, Menashe
CS Department of Cancer Biology, University of Texas M. D. Anderson Cancer Center, Houston, TX, 77054, USA
SO Clinical Cancer Research (2002), 8(11), 3584-3591
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB Purpose: Osteosarcoma is an aggressive primary bone cancer characterized by expression of **platelet**-derived growth factor (PDGF) and its cognate receptor. Coexpression of the growth factor and receptor suggests their role in autocrine or paracrine growth mechanisms. It has been reported previously that STI 571 has specific activity in inhibiting select tyrosine kinase receptors, including PDGF and c-Kit. Osteosarcomas express low levels of c-Kit but abundant levels of PDGF receptor (PDGFR). Exptl. Design: To investigate the potential of STI 571 as therapy for

osteosarcoma, we studied its effects on PDGF-mediated cell growth in vitro and in an in vivo mouse model. Results: PDGF acted as a potent mitogen in a dose-dependent manner in two osteosarcoma cell lines. STI 571 (1.0 μM) inhibited both PDGFR-α and PDGFR-β phosphorylation and the downstream phosphorylation targets extracellular signal-regulated kinase and Akt. STI 571 also inhibited PDGF-mediated growth and induced apoptosis in vitro as determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay and terminal deoxynucleotidyl transferase-mediated nick end labeling staining. To study the effect of STI 571 alone or in combination with Taxol in an in vivo model, an osteosarcoma cell line (KRIB) was transplanted into the tibia of athymic nude mice. Mice were treated with STI 571 (50 mg/kg p.o. q M-F), Taxol (8 mg/kg i.p. weekly), or STI 571 plus Taxol for 6 wk. There was no significant difference in tumor size between treatment and control mice. Aberrant signaling pathways downstream of the PDGFR in the v-Ki-ras oncogene-transformed KRIB cell line may in part explain this finding. Conclusions: Our data demonstrate that STI 571 inhibits PDGF-mediated growth and leads to apoptosis of osteosarcoma cells in vitro by selective inhibition of the PDGFR tyrosine kinase. The effectiveness of STI 571 in our studies suggests targeting of PDGFRs as a novel treatment for osteosarcoma.

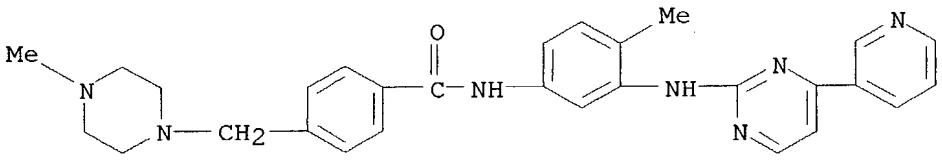
IT **220127-57-1,** STI 571
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571 inhibition of PDGF-mediated proliferation of osteosarcoma cells and mechanisms therein)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

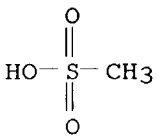
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

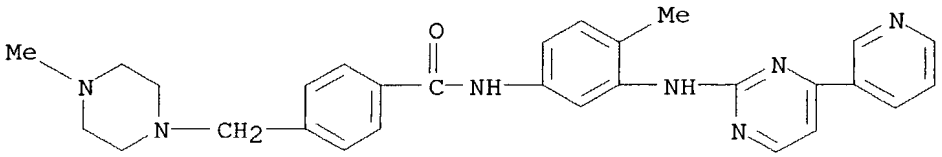


RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 71 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:906672 CAPLUS
DN 138:11199
TI Clinical course of thrombocytopenia in patients treated with imatinib mesylate for accelerated phase chronic myelogenous leukemia
AU van Deventer, Hendrik W.; Hall, Melissa D.; Orlowski, Robert Z.; Mitchell, Beverly S.; Berkowitz, Lee R.; Hogan, Cathe; Dunphy, Cherie H.; Koehler, Julie; Shea, Thomas C.
CS Department of Medicine, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
SO American Journal of Hematology (2002), 71(3), 184-190
CODEN: AJHEDD; ISSN: 0361-8609
PB Wiley-Liss, Inc.
DT Journal
LA English
AB We studied 28 patients with accelerated phase chronic myelogenous leukemia (CML) who were enrolled on the Novartis expanded access study 114. Diagnosis of accelerated phase CML was based on karyotypic evolution (n = 9) and hematol. criteria (n = 18). All patients were begun on 600 mg/day of imatinib mesylate. Dose redns. to 400 mg/day and then 300 mg/day were prescribed for an absolute neutrophil count (ANC) of <0.5/μl or a **platelet** count of <20,000/μl. Twenty-seven of the 28 patients continued treatment for a median of 34 wk. Eleven patients developed thrombocytopenia following an average of 8.4±1.4 wk of therapy. The onset of thrombocytopenia was associated with disease progression in one patient and a decline in bone marrow megakaryocytes in the other 10. Nine patients recovered to a **platelet** count of >20,000/μl after an average of 19.7±1.8 wk. Patients who developed thrombocytopenia had a longer duration of disease (9.39 vs. 4.35 yr; $P < 0.01$) and were more likely to be diagnosed with accelerated phase CML by hematol. criteria. Hematol. responses in patients with and without thrombocytopenia were comparable; however, 31.3% of patients without thrombocytopenia had a complete cytogenetic response compared to none of those with thrombocytopenia. Grade III-IV thrombocytopenia is common in accelerated phase CML and may be a marker for the inability to achieve cytogenetic response using single agent imatinib mesylate.
IT **220127-57-1**, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. course of thrombocytopenia in patients treated with imatinib mesylate for accelerated phase chronic myelogenous leukemia)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

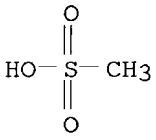
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



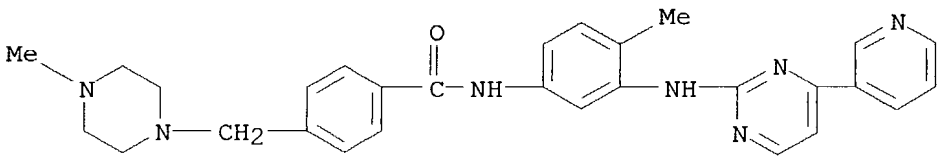
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 72 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:895959 CAPLUS
DN 137:379574
TI STI-571 in chronic myelogenous leukemia
AU Tsao, Anne S.; Kantarjian, Hagop; Talpaz, Moshe
CS Department of Bioimmunotherapy, M D Anderson Cancer Center, Houston, TX, USA
SO British Journal of Haematology (2002), 119(1), 15-24
CODEN: BJHEAL; ISSN: 0007-1048
PB Blackwell Science Ltd.
DT Journal; General Review
LA English
AB A review. STI-571 (imatinib mesylate) is the prototype for signal transduction inhibitors. It is the model for rational drug design, in that it targets the genetic mutation of the disease. STI-571, a 2-phenylaminopyrimidine, is a highly selective inhibitor of the protein tyrosine kinase family, which includes BCR-ABL protein, the **platelet**-derived growth factor (PDGF) receptor and the c-kit receptor. Chronic myelogenous leukemia (CML) is a stem cell disorder characterized by the Philadelphia chromosome and is dependent on the constitutively active tyrosine kinase protein BCR-ABL. In the CML model, STI-571 competitively binds to the ATP-binding site of the BCR-ABL and inhibits protein tyrosine phosphorylation. This review begins with a historical overview of CML therapy, then discusses STI-571 and its impact in the treatment of CML via clin. trials. The second part of this review addresses the issue of CML resistance to STI-571. A summary of the currently known mechanisms of resistance and the available options to overcome resistant disease is reviewed.
IT **220127-57-1**, STI-571
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI-571 in chronic myelogenous leukemia patients)
RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

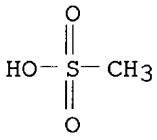
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 73 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:856282 CAPLUS
DN 137:345465
TI Imatinib mesylate (Gleevec/Glivec): a new therapy for chronic myeloid leukemia and other malignancies
AU Hernandez-Boluda, Juan Carlos; Cervantes, Francisco
CS Hematology and Medical Oncology Department, Hospital Clinico Universitario, Valencia, Spain
SO Drugs of Today (2002), 38(9), 601-613
CODEN: MDACAP; ISSN: 0025-7656
PB Prous Science
DT Journal; General Review
LA English
AB A review. Imatinib mesylate (STI571, Gleevec, Glivec), a selective inhibitor of the BCR-ABL tyrosine kinase causative of chronic myeloid leukemia (CML), represents the paradigm of how a better understanding of the pathogenetic mechanisms of a neoplastic disease can lead to the development of a targeted mol. therapy. Phase II clin. trials have shown marked therapeutic activity of imatinib in all evolutive phases of CML, but notably in the chronic phase, where it induces complete hematol. responses in almost 100% of patients resistant or intolerant to interferon, with a major cytogenetic response rate of 60%, including 41% complete cytogenetic responses. The preliminary results of an ongoing phase III multicenter randomized study comparing imatinib with interferon

plus cytarabine as first-line treatment for CML favor imatinib in terms of efficacy and safety. If confirmed with longer follow-up, these results would establish imatinib as the choice therapy for the majority of CML patients, with allogeneic transplantation being restricted as initial therapy only to younger patients with a family donor. Longer follow-up will answer some questions, such as those on long-term safety, durability of the responses, whether these will translate into a survival prolongation and the possibility of mol. responses. In addition, further information on the mechanisms involved in the primary and acquired resistance to imatinib is needed. Besides the Bcr-Abl protein, the drug is also active against other tyrosine kinases, such as Abl, the stem-cell factor receptor (c-kit) and the **platelet**-derived growth factor receptor, whose inhibition might have potential implications for the treatment of several malignancies. In this sense, it must be pointed out that imatinib has shown a remarkable activity in gastrointestinal stromal tumors.

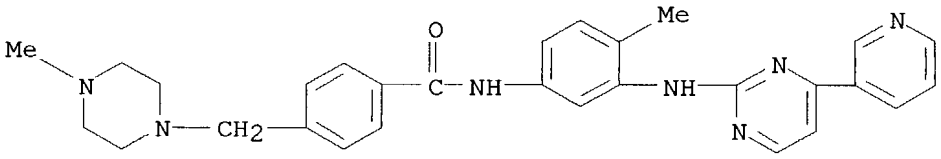
IT **220127-57-1**, Gleevec
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate (Gleevec/Glivec) for treatment of chronic myeloid leukemia and other malignancies)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

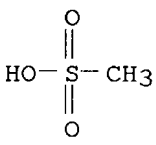
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



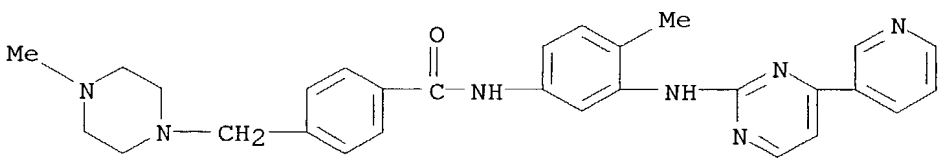
RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 74 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:779620 CAPLUS
DN 138:314057
TI Inhibition of PDGF receptor signaling in tumor stroma enhances antitumor effect of chemotherapy
AU Pietras, Kristian; Rubin, Kristofer; Sjoblom, Tobias; Buchdunger, Elisabeth; Sjoquist, Mats; Heldin, Carl-Henrik; Ostman, Arne
CS Ludwig Institute for Cancer Research, Uppsala, SE-751 24, Swed.
SO Cancer Research (2002), 62(19), 5476-5484
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Lowering of tumor interstitial hypertension, which acts as a barrier for tumor transvascular transport, has been proposed as a general strategy to enhance tumor uptake and therapeutic effects of anticancer drugs. The tyrosine kinase **platelet**-derived growth factor (PDGF) β-receptor is one mediator of tumor hypertension. The effects of PDGF antagonists on chemotherapy response were investigated in two tumor models that display PDGF receptor expression restricted to the tumor stroma, and in which PDGF antagonists relieve tumor hypertension. Inhibitory PDGF aptamers and the PDGF receptor tyrosine kinase inhibitor STI571 enhanced the antitumor effect of Taxol on s.c. KAT-4 tumors in SCID mice. Treatment with only PDGF antagonists had no effect on tumor growth. Taxol uptake in tumors was increased by treatment with PDGF antagonists. Cotreatment with PDGF antagonists and Taxol was not associated with antiangiogenic effects, and PDGF antagonists did not enhance the Taxol effect on in vitro growth of KAT-4 cells. STI571 also increased the antitumor effects of 5-fluorouracil on s.c. PROb tumors in syngeneic BDIX rats, without increasing the effect of 5-fluorouracil on cultured PROb cells. Expression of PDGF receptors in tumor stroma, as well as tumor hypertension, occurs in most common solid tumors. Therefore, our results have implications for treatment regimens for large patient groups and merit clin. testing. In conclusion, our study identifies inhibition of PDGF signaling in tumor stroma as a novel, possibly general strategy for enhancement of the therapeutic effects chemotherapy.
IT **220127-57-1**, STI 571
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of PDGF receptor signaling in tumor stroma enhances antitumor effect of chemotherapy)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

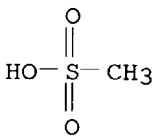
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

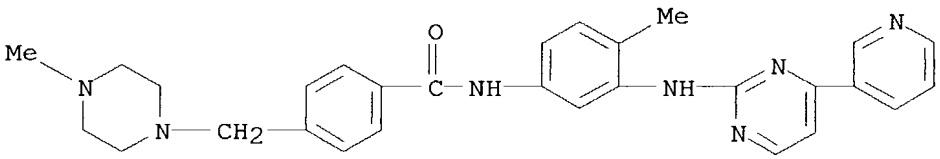


RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 75 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:731584 CAPLUS
DN 138:264989
TI Glivec: a new treatment modality for CML: a case history
AU Zimmermann, Jurg
CS Novartis Pharma AG Praklinische Forschung, Basel, CH-4002, Switz.
SO Chimia (2002), 56(7-8), 428-431
CODEN: CHIMAD; ISSN: 0009-4293
PB Schweizerische Chemische Gesellschaft
DT Journal; General Review
LA English
AB A review. Glivec (the brand name in the US is Gleevec) is a protein-tyrosine kinase inhibitor which potently inhibits the Abl tyrosine kinase in vitro and in vivo. The compound specifically inhibits proliferation of v-abl and bcr-abl expressing cells, suggesting that it is not a general antimitotic agent. In addition, Glivec is a potent inhibitor of the **platelet**-derived growth factor receptor kinase (PDGF-R) and of the receptor kinase for stem cell factor (SCF), c-Kit, and inhibits PDGF- and SCF-mediated biochem. events. In contrast, it does not affect signal transduction mediated by other stimuli including epidermal growth factor (EGF), insulin and phorbol esters. Pharmacokinetic studies in various animal species demonstrate that pharmacol. relevant concns. are achieved in the plasma following oral administration of the drug. STI571 shows antitumor activity as a single agent in animal models at well-tolerated doses. On May 10, 2001, the U.S. Food and Drug administration announced the fast track approval of Gleevec (imatinib mesylate), our treatment for patients with chronic myeloid leukemia (CML) in blast crisis, accelerated phase or chronic phase after failure of interferon-alpha therapy. The FDA approval came in just over 10 wk after Novartis filed its New Drug Application, and just two months after the FDA notified us that it had granted Glivec a priority review.
IT **220127-57-1**, Glivec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Glivec as treatment modality for CML)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

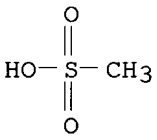
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 76 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:708401 CAPLUS
DN 138:331281
TI Molecular Targeting of **Platelet**-Derived Growth Factor B by Imatinib Mesylate in a Patient With Metastatic Dermatofibrosarcoma Protuberans
AU Rubin, Brian P.; Schuetze, Scott M.; Eary, Janet F.; Norwood, Thomas H.; Mirza, Sohail; Conrad, Ernest U.; Bruckner, James D.
CS Dep. Pathol., Med., Nucl. Med., Orthoped., University of Washington Medical Center, Seattle, WA, USA
SO Journal of Clinical Oncology (2002), 20(17), 3586-3591
CODEN: JCONDN; ISSN: 0732-183X
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Dermatofibrosarcoma protuberans is caused by activation of the **platelet**-derived growth factor B (PDGFB) receptor, a transmembrane tyrosine kinase. We investigated the response of dermatofibrosarcoma protuberans to the tyrosine kinase inhibitor imatinib mesylate. A patient with unresectable, metastatic dermatofibrosarcoma protuberans received imatinib mesylate (400 mg bid). Response to therapy was assessed by [18F]fluorodeoxyglucose (FDG) positron emission tomog., magnetic, resonance imaging, and histopathol. and immunohistochem. evaluation. The patient was treated for 4 mo with imatinib mesylate. The hypermetabolic uptake of FDG fell to background levels within 2 wk of treatment, and the tumor volume shrank by over 75% during the 4 mo of therapy, allowing for resection of the mass. There was no residual viable tumor in the resected specimen, indicating a complete histol. response to treatment with imatinib mesylate. Thus, imatinib mesylate is highly active in dermatofibrosarcoma protuberans. The dramatic response seen in this

patient demonstrates that inhibition of PDGFB receptor tyrosine kinase activity can significantly impact viability of at least one type of solid tumor.

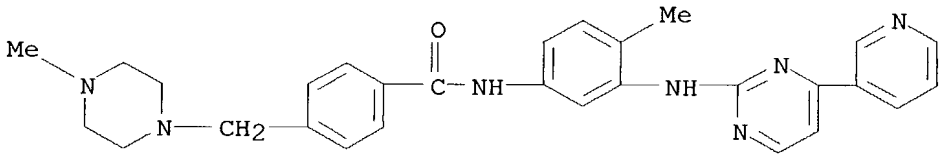
IT **220127-57-1**, Imatinib mesylate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. targeting of **platelet**-derived growth factor B by imatinib mesylate in a patient with metastatic dermatofibrosarcoma protuberans)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

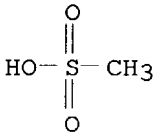
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 77 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:675840 CAPLUS
DN 137:226590
TI Use of epothilone derivatives and a signal transduction inhibitor for the treatment of cancer
IN Buchdunger, Elisabeth; Heldin, Carl-Henrik; Oestman, Arne; Pietras, Kristian; O'Reilly, Terence; Rothermel, John David; Traxler, Peter; Wartmann, Markus
PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Brandt, Ralf
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002067941	A2	20020906	WO 2002-EP2049	20020226
	WO 2002067941	A3	20031120		
	WO 2002067941	C1	20031218		
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	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
				GB 2001-4840 A	20010227
				US 2001-339040PP	20011030
	EP 1385522	A2	20040204	EP 2002-744903	20020226
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
				GB 2001-4840 A	20010227
				US 2001-339040PP	20011030
				WO 2002-EP2049 W	20020226
	BR 2002007649	A	20040309	BR 2002-7649	20020226
				GB 2001-4840 A	20010227
				US 2001-339040PP	20011030
				WO 2002-EP2049 W	20020226
	NO 2003003769	A	20030825	NO 2003-3769	20030825
				GB 2001-4840 A	20010227
				US 2001-339040PP	20011030
				WO 2002-EP2049 W	20020226

OS MARPAT 137:226590

AB The present invention relates to a combination which comprises (a) a signal transduction inhibitor selected from a PDGF (**platelet** -derived growth factor) receptor tyrosine kinase inhibitor which is a N-phenyl-2-pyrimidine-amine derivative such as I [R1 = pyrazinyl, pyrrolyl, substituted phenyl; R2, R3 = H, alkyl; R4, R5, R6, R7, R8 = nitro, alkoxy, -N(R9)-C(=X)-(Y)n-R10; R9 = H, alkyl; X = oxo, thio, imino, N-alkylamino, hydroximino; Y = O, NH; n = 0, 1; R10 = alkyl, aryl, cycloalkyl, heterocycle], and an active ingredient which decreases the activity of the epidermal growth factor (EGF) and (b) an epothilone derivative such as II [A = O, NRn; Rn = H, alkyl; R = H, alkyl; Z = O, a bond], and optionally at least one pharmaceutically acceptable carrier for simultaneous, sep. or sequential use, in particular, for the delay of progression or treatment of a proliferative disease. The invention also discloses a com. package comprising such a combination as a combined preparation and to a method of treatment of a warm-blooded animal, especially human.

IT **220127-57-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; use of epothilone derivs. and a signal transduction inhibitor for the treatment of cancer)

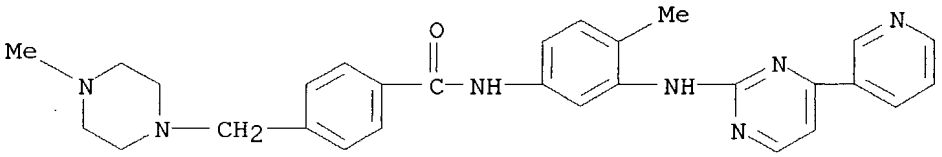
RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

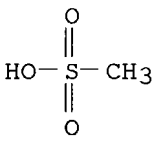
CRN 152459-95-5

CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 78 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:609456 CAPLUS
DN 137:210576
TI Response to imatinib mesylate in patients with chronic myeloproliferative diseases with rearrangements of the **platelet**-derived growth factor receptor beta
AU Apperley, Jane F.; Gardembas, Martine; Melo, Junia V.; Russell-Jones, Robin; Bain, Barbara J.; Baxter, E. Joanna; Chase, Andrew; Chessells, Judith M.; Colombat, Marie; Dearden, Claire E.; Dimitrijevic, Sasa; Mahon, Francois-X.; Marin, David; Nikolova, Zariana; Olavarria, Eduardo; Silberman, Sandra; Schultheis, Beate; Cross, Nicholas C. P.; Goldman, John M.
CS Dep. Haematology, Fac. Med., Imperial College, London, W12 0NN, UK
SO New England Journal of Medicine (2002), 347(7), 481-487
CODEN: NEJMAG; ISSN: 0028-4793
PB Massachusetts Medical Society
DT Journal
LA English
AB A small proportion of patients with chronic myeloproliferative diseases have constitutive activation of the gene for **platelet**-derived growth factor receptor beta (PDGFRB), which encodes a receptor tyrosine kinase. The gene is located on chromosome 5q33, and the activation is usually caused by a t(5;12)(q33;p13) translocation associated with an ETV6-PDGFRB fusion gene. The tyrosine kinase inhibitor imatinib mesylate specifically inhibits ABL, PDGFR, and KIT kinases and has impressive clin. efficacy in BCR-ABL-pos. chronic myeloid leukemia. We treated four patients who had chronic myeloproliferative diseases and chromosomal translocations involving 5q33 with imatinib mesylate (400 mg daily). Three of the four patients presented with leukocytosis and eosinophilia; their leukemia cells carried the ETV6-PDGFRB fusion gene. The fourth patient had leukocytosis, eosinophilia, and a t(5;12) translocation involving PDGFRB and an unknown partner gene; he also had extensive raised, ulcerated skin lesions that had been present for a long time. In

all four patients, a normal blood count was achieved within four weeks after treatment began. In the patient with skin disease, the lesions began to resolve shortly after treatment began. The t(5;12) translocation was undetectable by 12 wk in three patients and by 36 wk in the fourth patient. In the three patients with the ETV6-PDGFRB fusion gene, the transcript level decreased, and in one patient, it became undetectable by 36 wk. All responses were durable at 9 to 12 mo of follow-up. Imatinib mesylate induces durable responses in patients with chronic myeloproliferative diseases associated with activation of PDGFRB.

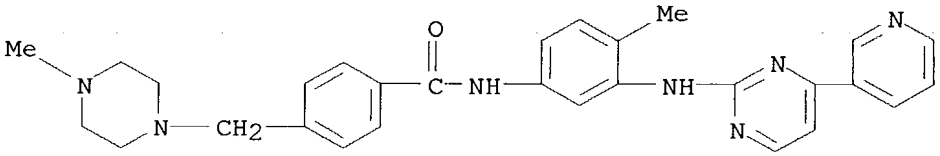
IT **220127-57-1**, Imatinib mesylate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate in patients with chronic myeloproliferative diseases with rearrangements of **platelet**-derived growth factor receptor beta)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

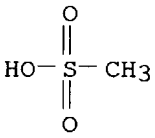
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



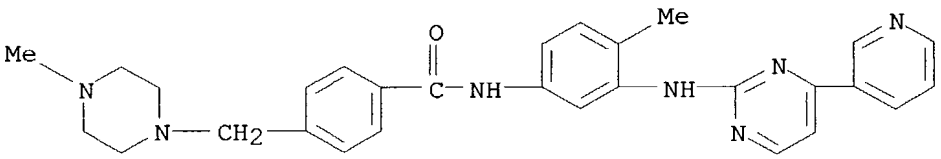
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 79 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:596293 CAPLUS
DN 137:179525
TI Differential sensitivity to imatinib of 2 patients with metastatic sarcoma arising from dermatofibrosarcoma protuberans
AU Maki, Robert G.; Awan, Rashid A.; Dixon, Richard H.; Jhanwar, Suresh; Antonescu, Cristina R.
CS Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York,

NY, 10021-6007, USA
SO International Journal of Cancer (2002), 100(6), 623-626
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Dermatofibrosarcoma protuberans (DFSP) is a rare superficial sarcoma usually affecting the trunk, with significant risk of local recurrence. It is characterized by the presence of ring chromosomes or chromosomal translocations fusing the promoter of the collagen gene COLIAI to the **platelet**-derived growth factor β-chain gene PDGFB, increasing the production of PDGF locally and promoting autocrine or paracrine tumor growth. Fewer than 5% of patients with DFSP develop metastatic sarcoma, with a poor subsequent prognosis. Imatinib (STI-571) was developed as an inhibitor of the PDGF receptor tyrosine kinase and has proven clin. activity against chronic myelogenous leukemia (expressing bcr-abl) and gastrointestinal stromal tumors (expressing c-kit). We describe 2 patients with metastatic and unresectable metastases from DFSP treated with imatinib. After confirmation of neg. CD117 status of 2 sarcomas arising from DFSP, patients were given imatinib 400 mg po qd and assessed at regular intervals for their tolerance and response to therapy. One patient had a transient response, then progressed rapidly and died of disease. Another patient showed a partial response to therapy after 2 mo, with resolution of superior vena cava syndrome and shrinking of metastatic lung lesions. His response is ongoing after 6 mo of therapy. These clin. data confirm findings from models of DFSP and support the use of imatinib in the rare setting of metastatic DFSP. Imatinib may be useful for patients with locally advanced DFSP, when other options for local therapy are limited.
IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; differential sensitivity to imatinib of 2 patients with metastatic sarcoma arising from dermatofibrosarcoma protuberans)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

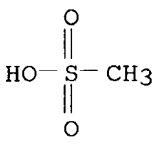
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

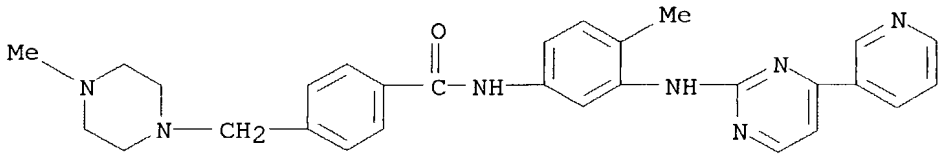


RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 80 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:574614 CAPLUS
DN 137:134358
TI Clinical management of gastrointestinal stromal tumors: Before and after STI-571
AU Dematteo, Ronald P.; Heinrich, Michael C.; El-Rifai, Wa'el M.; Demetri, George
CS Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SO Human Pathology (2002), 33(5), 466-477
CODEN: HPCQA4; ISSN: 0046-8177
PB W. B. Saunders Co.
DT Journal; General Review
LA English
AB A review. Gastrointestinal stromal tumor (GIST) is the most common mesenchymal neoplasm of the gastrointestinal tract. Until recently, surgery has been the only effective therapy for GIST. However, even after complete resection of tumor, many patients still eventually die of disease recurrence. Conventional chemotherapy and radiation therapy have been of limited value. Within the last few years, it was discovered that most GISTs have a gain-of-function mutation in the c-kit proto-oncogene. This results in ligand-independent activation of the KIT receptor tyrosine kinase and an unopposed stimulus for cell growth. STI-571 is a small mol. that selectively inhibits the enzymic activity of the ABL, **platelet**-derived growth factor receptor, and KIT tyrosine kinases and the BCR-ABL fusion protein and is a landmark development in cancer therapy. Its clin. development marks a new era of rational and targeted mol. inhibition of cancer that emanates from direct collaborations between scientists and clinicians. It provides proof of the principle that a specific mol. inhibitor can drastically and selectively alter the survival of a neoplastic cell with a particular genetic aberration. The advent of STI-571 has markedly altered the clin. approach to GIST. It has proven to be effective in metastatic GIST and is also under investigation as a neoadjuvant and adjuvant therapy.
IT **220127-57-1**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; clin. management of patients with gastrointestinal stromal tumors: before and after STI-571)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
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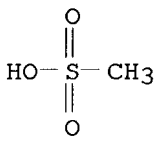


RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 81 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:569415 CAPLUS
DN 138:348357
TI c-KIT-expressing Ewing tumour cells are insensitive to imatinib mesylate (STI571)
AU Hotfilder, Marc; Lanvers, Claudia; Juergens, Heribert; Boos, Joachim; Vormoor, Josef
CS Department of Pediatric Hematology and Oncology, University of Muenster, University Children's Hospital Muenster, Muenster, 48129, Germany
SO Cancer Chemotherapy and Pharmacology (2002), 50(2), 167-169
CODEN: CCPHDZ; ISSN: 0344-5704
PB Springer-Verlag
DT Journal
LA English
AB In order to determine whether Ewing tumor patients may be potential candidates for imatinib mesylate therapy, we analyzed the expression of the currently known imatinib mesylate-sensitive tyrosine kinases and tested sensitivity to imatinib mesylate in a panel of eight Ewing tumor cell lines in vitro. Expression of the different tyrosine kinases was assessed by flow cytometry and RT-PCR. Sensitivity to imatinib mesylate was analyzed using a standard MTT proliferation assay. Flow cytometric and RT-PCR analyses in a panel of eight Ewing tumor cell lines demonstrated expression of several imatinib mesylate-sensitive tyrosine kinases, including c-KIT, **platelet**-derived growth factor receptor, c-ABL and c-ARG. However, in the MTT proliferation assay, all eight Ewing tumor cell lines were found to be resistant to imatinib mesylate at concns. ranging from 0.1 to 10 μM. Despite the expression of imatinib mesylate-sensitive tyrosine kinases, Ewing tumor cells proved resistant to imatinib mesylate in vitro. This observation has implications for the selection of patients for exptl. therapy with imatinib mesylate.
IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

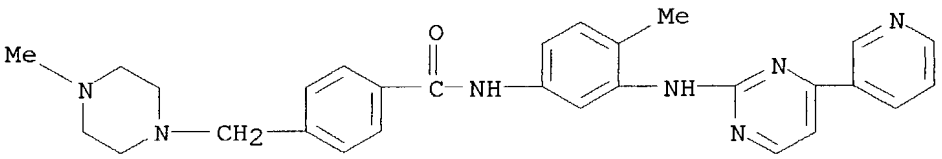
(Biological study); USES (Uses)
(resistance; c-KIT-expressing Ewing sarcoma tumor cells are insensitive to imatinib mesylate (STI571))

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

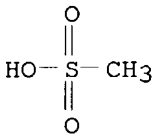
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 82 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:485661 CAPLUS

DN 137:88027

TI Chronic myelogenous leukemia in T cell lymphoid blastic phase achieving durable complete cytogenetic and molecular remission with imatinib mesylate (STI571; Gleevec) therapy

AU Atallah, Ehab; Talpaz, Moshe; O'Brien, Susan; Rios, Mary Beth; Guo, Jie Qiang; Arlinghaus, Ralph; Fernandes-Reese, Sofia; Kantarjian, Hagop

CS Department of Leukemia, University of Texas M. D. Anderson Cancer Center, Houston, TX, USA

SO Cancer (New York, NY, United States) (2002), 94(11), 2996-2999
CODEN: CANCAR; ISSN: 0008-543X

PB John Wiley & Sons, Inc.

DT Journal

LA English

AB A T cell lymphoid blastic phase of chronic myelogenous leukemia (CML) is a rare occurrence, with only a few reported cases worldwide. Standard therapy for such patients is undetd. Imatinib mesylate, a Bcr-Abl tyrosine kinase inhibitor, has shown activity in CML. The authors report on a patient with CML and marrow as well as extramedullary nodal T cell lymphoid

blastic phase who was treated with imatinib mesylate. The patient achieved complete morphol. and cytogenetic remission within two months of therapy. Competitive quant. polymerase chain reaction anal. of marrow cells was neg. after 15 mo. Response had lasted for 26+ months at the time of writing. The current data suggest that imatinib mesylate may produce long-term event free survival in patients with T-cell lymphoid blastic phase CML. Its potential role alone or in combinations should be further explored in this condition.

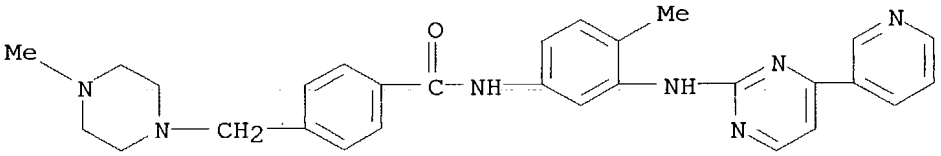
IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate therapy: complete cytogenetic and mol. remission in chronic myelogenous leukemia patients in T cell lymphoid blastic phase)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

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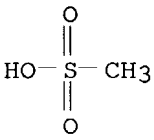

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 83 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:395649 CAPLUS
DN 138:32590
TI STI571 (glivec): A new paradigm for the development of innovative therapies in onco-hematology?
AU Gambacorti, Carlo
CS Department of Experimental Oncology, National Cancer Institute, Milan, 20133, Italy
SO Tumori (2001), 87(6), S10-S12
CODEN: TUMOAB; ISSN: 0300-8916

PB Il Pensiero Scientifico Editore
DT Journal; General Review
LA English
AB A review. STI571 is a rationally developed, potent, and selective inhibitor for abl tyrosine kinases, including Bcr-Abl, as well as c-kit and the **platelet**-derived growth factor receptor tyrosine kinases. STI571 has been selected as an inhibitor of Bcr/Abl, an oncogenic fusion protein known to cause chronic myelogenous leukemia (CML). CML is a clonal hematopoietic stem cell disorder with an incidence of one to two cases per 100,000 per yr. It progresses through distinct phases: the stable or chronic phase, the accelerated phase, and the blast crisis. The chronic phase is characterized by massive expansion of myeloid cells, which maintain normal maturation. In the later phases, leukemic cells lose their capacity to terminally differentiate, due to addnl. genetic lesions. The result is an acute leukemia, which is highly refractory to therapy.
IT **220127-57-1**, STI 571
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor activity of STI571 (glivec), an inhibitor of Bcr/Abl tyrosine kinase, in chronic myelogenous leukemia)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
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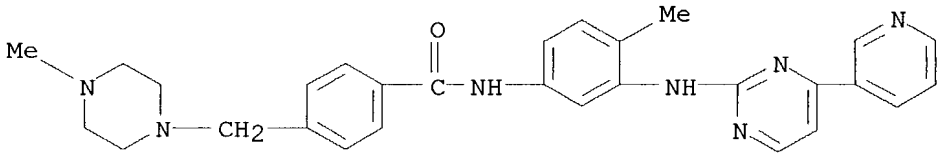

CM 2

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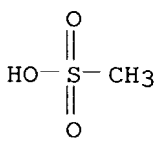


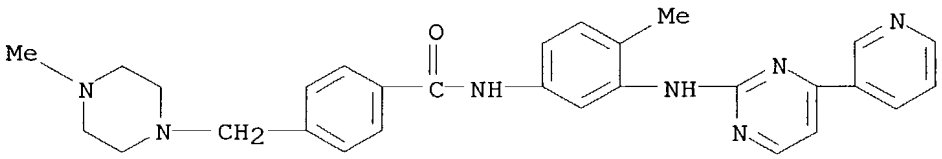
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 84 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:385493 CAPLUS
DN 137:358
TI Phase 2 trial of imatinib mesylate in myelofibrosis with myeloid metaplasia
AU Tefferi, Ayalew; Mesa, Ruben A.; Gray, Leigh A.; Steensma, David P.; Camoriano, John K.; Elliott, Michelle A.; Pardanani, Animesh; Ansell, Stephen M.; Call, Timothy G.; Colon-Otero, Gerardo; Schroeder, Georgene; Hanson, Curtis A.; Dewald, Gordon W.; Kaufmann, Scott H.
CS Mayo Clinic, Rochester, MN, 55905, USA
SO Blood (2002), 99(10), 3854-3856
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB In a phase 2 study, 23 patients with myelofibrosis with myeloid metaplasia were treated with imatinib mesylate at a constant dose of 400 mg/d. Treatment was held in 16 patients (70%), after 1 to 12 wk, because of side effects (neutropenia, 6 patients; musculoskeletal pain, 5 patients; thrombocytosis, 4 patients; edema, 3 patients; diarrhea and hyperbilirubinemia, 1 patient). Including patients in whom retreatment at a reduced dose was possible, 11 patients (48%) were able to continue treatment beyond 3 mo. None of the patients experienced a response in anemia, and only 2 had partial responses in splenomegaly. A greater than 50% increase in **platelet** count was documented in 11 (48%) patients, but not in those with baseline **platelet** counts of less than 100 + 109/L. In vitro, imatinib mesylate caused variable degrees of growth suppression of myeloid and erythroid progenitors that unfortunately did not translate into clin. benefit.
IT **220127-57-1**, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate in myelofibrosis patients with myeloid metaplasia)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

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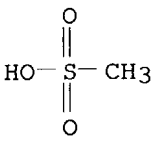
CMF C H4 O3 S



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 85 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:385411 CAPLUS
DN 137:357
TI Imatinib induces hematologic and cytogenetic responses in patients with chronic myelogenous leukemia in myeloid blast crisis: results of a phase II study
AU Sawyers, Charles L.; Hochhaus, Andreas; Feldman, Eric; Goldman, John M.; Miller, Carole B.; Ottmann, Oliver G.; Schiffer, Charles A.; Talpaz, Moshe; Guilhot, Francois; Deininger, Michael W. N.; Fischer, Thomas; O'Brien, Steve G.; Stone, Richard M.; Gambacorti-Passerini, Carlo B.; Russell, Nigel H.; Reiffers, Jose J.; Shea, Thomas C.; Chapuis, Bernard; Coutre, Steven; Tura, Sante; Morra, Enrica; Larson, Richard A.; Saven, Alan; Peschel, Christian; Gratwohl, Alois; Mandelli, Franco; Ben-Am, Monique; Gathmann, Insa; Capdeville, Renaud; Paquette, Ronald L.; Druker, Brian J.
CS Department of Medicine and Molecular Biology Institute, University of California, Los Angeles, CA, 90095, USA
SO Blood (2002), 99(10), 3530-3539
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Blast crisis is the most advanced stage of chronic myelogenous leukemia (CML) and is highly refractory to therapy. CML is caused by expression of the chimeric BCR-ABL tyrosine kinase oncogene, the product of the t(9;22) Philadelphia translocation. Imatinib (Glivec, formerly STI571) is a rationally developed, orally administered inhibitor of the Bcr-Abl tyrosine kinase. A total of 260 patients with CML were enrolled in a phase II trial, of whom 229 had a confirmed diagnosis of CML in blast crisis. Patients were treated with imatinib in daily oral doses of 400 mg or 600 mg. Imatinib induced hematol. responses in 52% of patients and sustained hematol. responses lasting at least 4 wk in 31% of patients, including complete hematol. responses in 8%. For patients with a sustained response, the estimated median response duration was 10 mo. Imatinib induced major cytogenetic responses in 16% of patients, with 7% of the responses being complete. Median survival time was 6.9 mo. Nonhematol. adverse reactions were frequent but generally mild or moderate. Episodes of severe cytopenia were also frequent and were attributable to the underlying condition and treatment with imatinib. Drug-related adverse events led to discontinuation of therapy in 5% of patients, most often because of cytopenia, skin disorders, or gastrointestinal reactions. These results demonstrate that imatinib has substantial activity and a favorable safety profile when used as a single agent in patients with CML in blast crisis. Addnl. clin. studies are warranted to explore the efficacy and feasibility of imatinib used in combination with other antileukemic drugs.
IT **220127-57-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

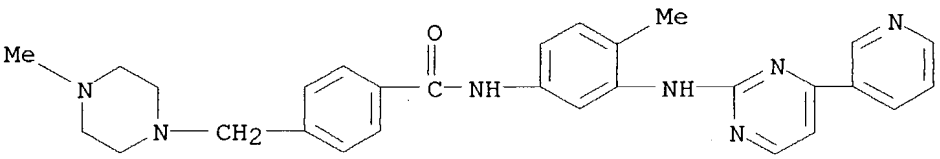
(imatinib, BCR-ABL tyrosine kinase inhibitor, induces hematol. and cytogenetic responses in chronic myelogenous leukemia patients in myeloid blast crisis)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

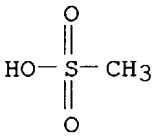
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 86 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:275806 CAPLUS

DN 136:304047

TI Effects of combined administration of farnesyl transferase inhibitors and signal transduction inhibitors

IN Daley, George Q.; Hoover, Russell R.

PA Whitehead Institute for Biomedical Research, USA

SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002028409	A2	20020411	WO 2001-US31104	20011004
	WO 2002028409	A3	20030306		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,

PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

			US	2000-238240PP 20001005
			US	2000-238813PP 20001006
AU	2002011427	A5	20020415	AU 2002-11427 20011004
			US	2000-238240PP 20001005
			US	2000-238813PP 20001006
			WO	2001-US31104W 20011004
US	2002077301	A1	20020620	US 2001-971365 20011004
			US	2000-238240PP 20001005
			US	2000-238813PP 20001006

PATENT FAMILY INFORMATION:
FAN 2002:275781

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002028381	A2	20020411	WO 2001-US42509	20011005
	WO 2002028381	A3	20030327		

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CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU,
ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK,
SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ,
MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

			US	2000-238240PP 20001005
AU	2002011862	A5	20020415	AU 2002-11862 20011005
			US	2000-238240PP 20001005
			WO	2001-US42509W 20011005
US	2002128280	A1	20020912	US 2001-971545 20011005
			US	2000-238240PP 20001005
EP	1322334	A2	20030702	EP 2001-979952 20011005

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

			US	2000-238240PP 20001005
			WO	2001-US42509W 20011005
BR	2001014430	A	20040106	BR 2001-14430 20011005
			US	2000-238240PP 20001005
			WO	2001-US42509W 20011005
JP	2004510733	T2	20040408	JP 2002-532206 20011005
			US	2000-238240PP 20001005
			WO	2001-US42509W 20011005
NO	2003001531	A	20030605	NO 2003-1531 20030404
			US	2000-238240PP 20001005
			WO	2001-US42509W 20011005

AB The invention relates to methods of reducing proliferation of cells, enhancing apoptosis of cells or both in an individual in need thereof, comprising administering to the individual a combination of at least one farnesyl transferase inhibitor (FTI), such as an inhibitor or Ras function, and at least one signal transduction inhibitor (STI) in a therapeutically effective amount, wherein proliferation of cells is reduced and/or apoptosis of cells in enhanced in the individual. The invention also discloses a method of reducing proliferation of STI resistant cells, enhancing apoptosis of STI resistant cells, or both in an individual in need thereof, comprising administering to the individual a combination of

at least one FTI and at least one STI in a therapeutically effective amount, wherein proliferation of STI resistant cells is reduced and/or apoptosis of STI resistant cells is enhanced in the individual. The invention can be used to treat leukemia (e.g., CML) using this combination of farnesyl transferase inhibitor and signal transduction inhibitor.

IT **220127-57-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; effects of combined administration of farnesyl transferase inhibitors and signal transduction inhibitors)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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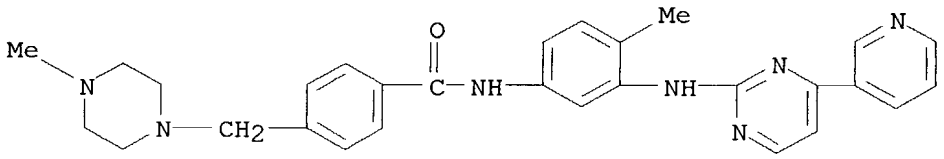
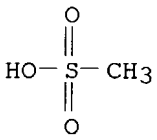
CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L17 ANSWER 87 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:241866 CAPLUS
DN 137:103258
TI STI571 (imatinib mesylate): the tale of a targeted therapy
AU Thambi, Paul; Sausville, Edward A.
CS Developmental Therapeutics Program, National Cancer Institute, Rockville, MD, 20852, USA
SO Anti-Cancer Drugs (2002), 13(2), 111-114
CODEN: ANTDEV; ISSN: 0959-4973
PB Lippincott Williams & Wilkins
DT Journal; General Review
LA English
AB A review. STI571 (imatinib mesylate) is an example of the successful development of a targeted agent. Its target is the constitutively active tyrosine kinase (p210bcr-abl) in a hematol. neoplasm, chronic myelogenous

leukemia (CML). The results in early clin. trials were remarkable and led to rapid approval by the Food and Drug Administration for clin. use of the STI571 in CML. This article reviews the pre-clin. and clin. development of this agent and also discusses some of the prevailing theories to explain the emerging problem of resistance. Future directions for this drug, possibly directed at other targets, are also discussed.

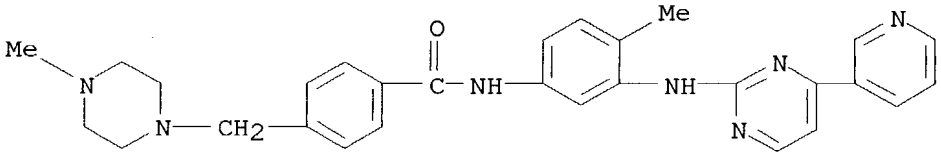
IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor imatinib mesylate)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

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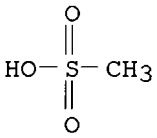

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 88 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:157004 CAPLUS
DN 137:225989
TI Imatinib mesylate - a new oral targeted therapy
AU Savage, David G.; Antman, Karen H.
CS Herbert Irving Comprehensive Cancer Center, Columbia Univ. College Physicians and Surgeons, New York, NY, USA
SO New England Journal of Medicine (2002), 346(9), 683-693
CODEN: NEJMAG; ISSN: 0028-4793
PB Massachusetts Medical Society
DT Journal; General Review
LA English
AB A review. Imatinib mesylate is an inhibitor of specific protein Tyr

kinases that was targeted to the **platelet**-derived growth factor receptor. It is highly active and has an acceptable level of toxicity when given alone for the treatment of chronic-phase chronic myelogenous leukemia (CML) and gastrointestinal stromal tumors. Imatinib has also limited activity against blast-phase CML and relapsed Philadelphia-chromosome-pos. acute lymphoblastic leukemia, conditions resistant to standard chemotherapy and even to allogeneic stem cell transplantation.

IT **220127-57-1,** Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib mesylate, a new oral targeted therapy)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
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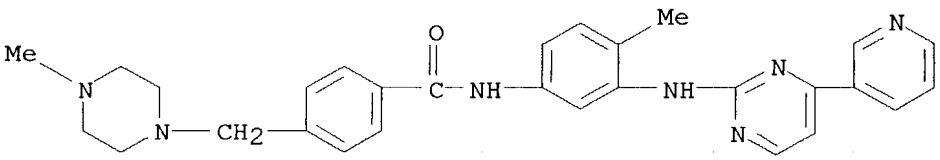

CM 2

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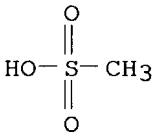

RE.CNT 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 89 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:132149 CAPLUS
DN 136:303452
TI STI571: a new treatment modality for CML?
AU Zimmermann, Jurg; Furet, Pascal; Buchdunger, Elisabeth
CS Pharma Research, Novartis, Basel, CH-4002, Switz.
SO ACS Symposium Series (2001), 796(Anticancer Agents), 245-259, 1 plate
CODEN: ACSMC8; ISSN: 0097-6156
PB American Chemical Society
DT Journal; General Review
LA English
AB A review. STI571 is a protein-tyrosine kinase inhibitor which potently

inhibits the Abl tyrosine kinase in vitro and in vivo. The compound specifically inhibits proliferation of v-abl and bcr-abl expressing cells, suggesting that it is not a general antimitotic agent. In addition, STI571 is a potent inhibitor of the **platelet**-derived growth factor receptor kinase (PDGF-R) and of the receptor kinase for stem cell factor (SCF), c-Kit, and inhibits PDGF- and SCF-mediated biochem. events. In contrast, it does not affect signal transduction mediated by other stimuli including epidermal growth factor (EGF), insulin and phorbol esters. Pharmacokinetic studies in various animal species demonstrate that pharmacol. relevant concns. are achieved in the plasma following oral administration of the drug. STI571 shows anti-tumor activity as a single agent in animal models at well tolerated doses. Promising data from phase I clin. trails in CML (chronic myeloid leukemia) patients support the notion that STI571 represents a new treatment modality for CML.

IT **220127-57-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; STI571 as new treatment modality for chronic myeloid leukemia which inhibits v-abl tyrosine kinase in relation to bcr-abl expression)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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CRN 152459-95-5
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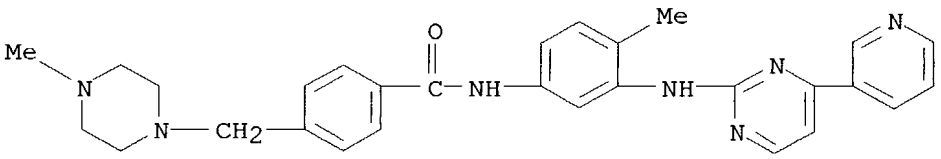

CM 2

CRN 75-75-2
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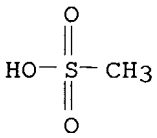

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 90 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:50995 CAPLUS
DN 137:119182
TI Effects of signal transduction inhibitor 571 in acute myelogenous leukemia

cells

AU Scappini, Barbara; Onida, Francesco; Kantarjian, Hagop M.; Li, Dong; Verstovsek, Srdan; Keating, Michael J.; Beran, Miloslav

CS Department of Leukemia, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA

SO Clinical Cancer Research (2001), 7(12), 3884-3893
CODEN: CCREF4; ISSN: 1078-0432

PB American Association for Cancer Research

DT Journal

LA English

AB STI571 is a 2-phenylalaminopyrimidine derivative that inhibits c-abl, Bcr-Abl, and **platelet**-derived growth factor receptor tyrosine kinases. Recently, inhibition of stem cell factor (SCF)-induced c-kit phosphorylation and cell proliferation by STI571 was reported in the human myeloid cell line MO7e. Because .apprx.70% of acute myelogenous leukemia (AML) cases are c-kit pos., the authors evaluated in vitro effects of STI571 on c-kit-pos. cell lines and primary AML blast cells. At concns. >5 μm, the drug marginally inhibited SCF-independent proliferation of cell lines and most of AML blasts. Treatment of AML cells with cytarabine and STI571 showed synergistic effect at low concns. Western blotting anal. documented a distinct band of Mr 145,000 specific for c-kit in cell lines and in AML samples. There was no correlation between the level of the c-kit expression evaluated by Western blotting and percentage of c-kit-pos. blasts as measured by flow cytometry. Neither in cell lines nor in primary AML cells, c-kit autophosphorylation was detectable under standard growth conditions. SCF-induced phosphorylation of c-kit in MO7e cells was inhibited by STI571. In a c-kit-pos. AML-4 cell line, as well as in AML samples, c-kit phosphorylation was not induced by SCF exposure, suggesting that in these cases, the receptor could not be functionally activated. In conclusion, with the exception of MO7e, SCF did not induce phosphorylation of c-kit, and cell proliferation was not modulated in the presence of STI571. The authors did not detect any SCF-independent c-kit phosphorylation in the exptl. systems. Consequently, STI571 exerted only a limited inhibitory effect on the cell growth.

IT **220127-57-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; effects of signal transduction inhibitor 571 in human acute myelogenous leukemia cells in relation to stem cell factor-induced c-kit phosphorylation)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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CRN 152459-95-5
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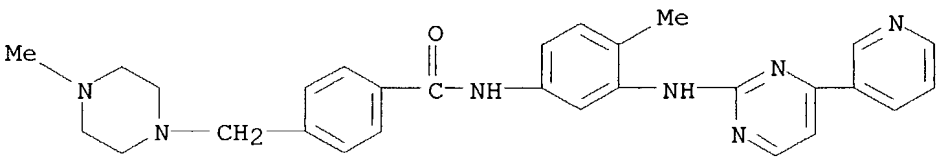

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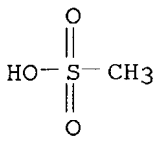

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 91 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:41569 CAPLUS
DN 136:318645
TI Rational therapeutic intervention in cancer: kinases as drug targets
AU Sawyers, Charles L.
CS Los Angeles Division of Hematology and Oncology, University of California, Los Angeles, CA, 90095-1678, USA
SO Current Opinion in Genetics & Development (2002), 12(1), 111-115
CODEN: COGDET; ISSN: 0959-437X
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
AB A review. Landmark clin. studies of new drugs developed to target specific forms of cancer were reported in 2001. Herceptin, a monoclonal antibody against the Her2/neu receptor tyrosine kinase, prolonged the survival of women with Her-2/neu pos. metastatic breast cancer, when combined with chemotherapy. STI-571, a small mol. inhibitor of the Bcr-Abl, c-kit and **platelet** derived growth factor receptor tyrosine kinases, produced dramatic clin. responses in patients with Bcr-Abl pos. chronic myeloid leukemia and c-kit pos. gastrointestinal stromal tumors. These examples have galvanized the cancer research community to extend kinase-inhibitor therapy to other cancers.
IT **220127-57-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; kinases as anticancer drug targets)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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CRN 152459-95-5
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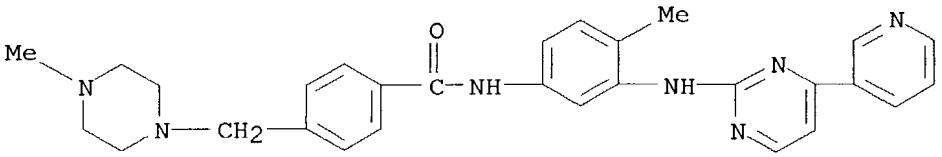

CM 2

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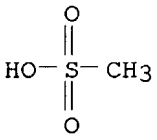

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 92 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:926227 CAPLUS
DN 136:193503
TI Tyrosine kinase inhibitor imatinib (STI571) as an anticancer agent for solid tumours
AU Joensuu, Heikki; Dimitrijevic, Sasa
CS Department of Oncology and Radiotherapy, Helsinki University Central Hospital, Helsinki, 00029, Finland
SO Annals of Medicine (Helsinki, Finland) (2001), 33(7), 451-455
CODEN: ANMDEU; ISSN: 0785-3890
PB Royal Society of Medicine Press Ltd.
DT Journal; General Review
LA English
AB A review. Imatinib mesylate, also known as STI571 or CGP57148, is a competitive inhibitor of a few tyrosine kinases, including BCR-ABL, ABL, KIT, and the **platelet**-derived growth factor receptors (PDGF-R). It binds to the ATP-binding site of the target kinase and prevents the transfer of phosphate from ATP to the tyrosine residues of various substrates. At oral doses of 300 mg or greater, the vast majority of patients with chronic myeloid leukemia achieve a haematol. response and this is usually associated with limited toxicity. Imatinib also has substantial activity in Philadelphia chromosome-pos. acute lymphoblastic leukemia expressing the BCR-ABL fusion protein. Gastrointestinal stromal tumors (GISTs) have also been evaluated for clin. activity of imatinib. About 90% of malignant GISTs harbor a mutation in c-kit leading to KIT receptor autophosphorylation and ligand-independent activation. According to initial clin. studies, more than 50% of GISTs respond to therapy within a few months, and only about 10-15% progress. The potential for cure and the optimal length of treatment are currently not known. Several other human cancers may over-express KIT or PDGF-R, and clin. trials to evaluate the role of imatinib in the treatment of such cancers are currently ongoing. Imatinib is an example of a specifically designed, highly targeted cancer therapy, which poses novel requirements for both pathol. labs. and clinicians in terms of identifying the major mol. mechanisms

involved in tumor growth.

IT **220127-57-1,** Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tyrosine kinase inhibitor imatinib (STI571) as anticancer agent for solid tumors)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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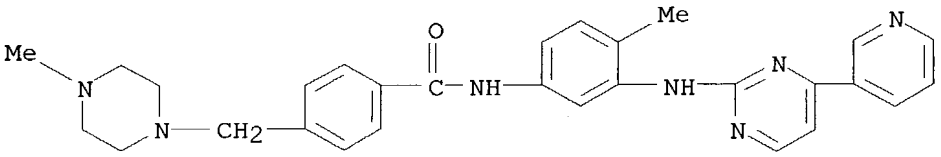
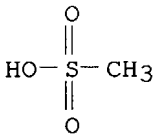


CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 93 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:839839 CAPLUS
DN 137:56743
TI Drugs targeted against protein kinases
AU Kumar, C. Chandra; Madison, Vincent
CS Departments of Tumour Biology and Structural Chemistry, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SO Expert Opinion on Emerging Drugs (2001), 6(2), 303-315
CODEN: EOEDA3
PB Ashley Publications Ltd.
DT Journal; General Review
LA English
AB A review. Current treatments for cancer (surgery, radiation and chemotherapy) are successful for early stage localized disease but have severe side effects. New treatments are needed to increase the cure rate and life expectancy of patients. With the discovery of oncogenes, tumor suppressor genes and an understanding of their role in the development of

the malignant disease, a new era of therapy has begun. Cancer is a manifestation of deregulated signaling pathways that mediate cell growth and programmed cell death. Protein kinases are essential elements in these signaling pathways. In the US, Novartis launched Gleevec (imantinib, STI-571) in May 2001 as the first anticancer drug whose mechanism of action is kinase inhibition. In Phase I trials, 23/24 patients with chronic myelogenous leukemia (CML) had complete remissions and the drug is relatively non-toxic. Herceptin (trastuzumab) is a monoclonal antibody (mAb) against a member of the growth factor receptor family (HER-2/neu) that was launched in 1998 by Genentech for the treatment of breast cancer. Trastuzumab has an excellent antitumor profile, particularly when used in combination with doxorubicin and paclitaxol. These drugs are pioneering the treatment of cancer based on the mol. understanding of the disease. Numerous drugs that target growth factor receptors and their signaling pathways are in advanced clin. trials. Herein, antibodies against receptors and small mol. inhibitors of kinases in signaling pathways will be summarized. Inter-disciplinary preclin. studies have identified chems. that target specific kinases. We believe that clin. studies of these agents will yield new anticancer agents that target specific diseases and that are less toxic than current agents.

IT **220127-57-1**, Gleevec
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; anticancer drugs targeted against protein kinases)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
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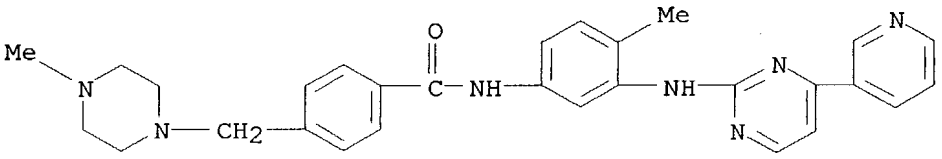

CM 2

CRN 75-75-2
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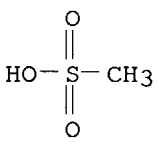


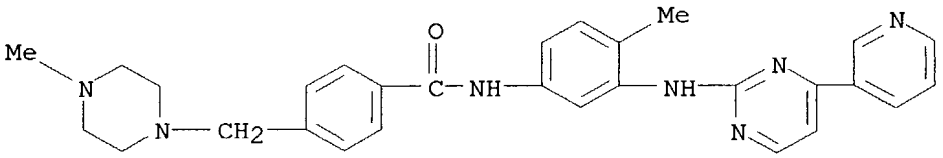
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 94 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:696815 CAPLUS
DN 136:66
TI Sarcoma
AU Maki, Robert
CS Memorial Sloan-Kettering Cancer Center, New York, NY, 10021-6007, USA
SO Oncologist (2001), 6(4), 333-337
CODEN: OCOLF6; ISSN: 1083-7159
PB AlphaMed Press
DT Journal; General Review
LA English
AB A review. ASCO 2001 was a banner year for innovative systemic therapy for sarcomas. Imatinib mesylate (STI571, Gleevec) shows clear activity not only in chronic myelogenous leukemia, for which the drug received Food and Drug Administration approval, but also in gastrointestinal stromal tumors as well, by virtue of imatinib mesylate binding to the abl, kit, and **platelet**-derived growth-factor receptor tyrosine kinases. Ecteinascidin-743 (ET-743) demonstrates activity against a fraction of other soft-tissue sarcomas. Gemcitabine-based regimens show at least some activity against a subset of soft-tissue sarcomas. Given the lack of new agents for sarcoma therapy since the development of ifosfamide, these studies give hope that the term "effective systemic therapy for sarcoma" might become a reality.
IT **220127-57-1**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; systemic therapy for sarcoma in humans)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

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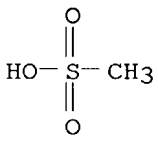
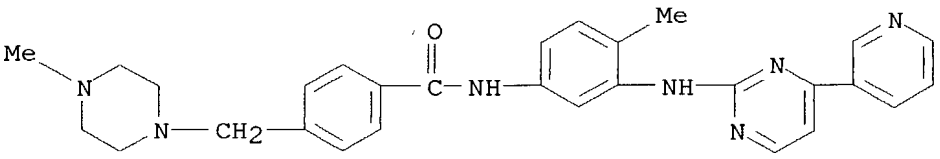


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 95 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:584373 CAPLUS
DN 135:338838
TI Growth inhibition of dermatofibrosarcoma protuberans tumors by the **platelet**-derived growth factor receptor antagonist STI571 through induction of apoptosis
AU Sjoblom, Tobias; Shimizu, Akira; O'Brien, Kevin P.; Pietras, Kristian; Dal Cin, Paola; Buchdunger, Elisabeth; Dumanski, Jan P.; Ostman, Arne; Heldin, Carl-Henrik
CS Ludwig Institute for Cancer Research, Uppsala, S-751 24, Swed.
SO Cancer Research (2001), 61(15), 5778-5783
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Dermatofibrosarcoma protuberans (DFSP) and giant cell fibroblastoma (GCF) are recurrent, infiltrative skin tumors that presently are treated with surgery. DFSP and GCF tumors are genetically characterized by chromosomal rearrangements fusing the collagen type 1α1 (COL1A1) gene to the **platelet**-derived growth factor B-chain (PDGFB) gene. It has been shown that the resulting COL1A1/PDGF-B fusion protein is processed to mature PDGF-BB. Autocrine PDGF receptor stimulation has therefore been predicted to contribute to DFSP and GCF tumor development and growth. Here we demonstrate presence of activated PDGF receptors in primary cultures derived from six different DFSP and GCF tumors. Three of the primary cultures were further characterized; their in vitro growth displayed an increased sensitivity to treatment with the PDGF receptor tyrosine kinase inhibitor STI571, as compared with normal fibroblasts. Transplantable tumors, displaying a DFSP-like histol., were established from one of the DFSP primary cultures. Treatment of tumor-bearing severe combined immunodeficient mice with STI571 reduced tumor growth. The growth-inhibitory effects in vitro and in vivo occurred predominantly through induction of tumor cell apoptosis. Our study demonstrates growth-inhibitory effects of PDGF receptor antagonists on human DFSP- and GCF-derived tumor cells and demonstrates that autocrine PDGF receptor stimulation provides antiapoptotic signals contributing to the growth of these cells. These findings suggest targeting of PDGF receptors as a novel treatment strategy for DFSP and GCF.
IT **220127-57-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; growth inhibition of dermatofibrosarcoma protuberans tumors by the **platelet**-derived growth factor receptor antagonist STI571 through induction of apoptosis)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

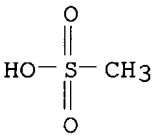
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 96 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:523289 CAPLUS
DN 135:312950
TI STI571: Targeting BCR-ABL as therapy for CML
AU Mauro, Michael J.; Druker, Brian J.
CS Leukemia Program, Division of Hematology and Medical Oncology, Oregon Health Sciences University, Portland, OR, 97201, USA
SO Oncologist (2001), 6(3), 233-238
CODEN: OCOLF6; ISSN: 1083-7159
PB AlphaMed Press
DT Journal; General Review
LA English
AB A review with refs. Therapeutic agent STI571 (signal transduction inhibitor number 571) is a rationally developed, potent, and selective inhibitor for abl tyrosine kinases, including bcr-abl, as well c-kit and the **platelet**-derived growth factor receptor tyrosine kinases. Results of clin. trials to date have demonstrated the crucial role of the bcr-abl tyrosine kinase in chronic myelogenous leukemia (CML) pathogenesis and the potential of anticancer agents designed to target specific mol. abnormalities in human cancer. An initial phase I study of STI571 included 83 Ph+ CML patients who had failed interferon-based therapy. Patients were required to be in chronic phase, defined liberally as less than 15% blasts in blood or bone marrow. Patients were treated with once-daily oral doses of STI571 in 14 successive dose cohorts ranging from 25-1,000 mg. In this phase I study, no dose-limiting toxicity was encountered and toxicity at all dose levels was minimal. The threshold for a maximally ED was found at 300 mg; for patients treated at or above this level, complete hematol. response was seen in 98% of patients, with complete cytogenetic responses in 13% and major cytogenetic responses in 31%. With a median duration of follow-up of 310 days, ongoing responses are evident in 96% of patients. In the phase II study of the accelerated phase of CML, 233 patients were treated with either 400 or 600 mg of STI571. With similar follow-up to the chronic phase trial, 91% of patients showed a hematol. response; 63% of patients achieved a complete

hematol. response but not all patients had recovery of peripheral blood counts. In addition to the phase II clin. trials with STI571, a phase III trial randomizing newly diagnosed patients to either interferon with low-dose s.c. cytosine arabinoside vs. STI571 is ongoing; this trial accrued rapidly and data collection is ongoing. Integration of STI571 into CML treatment algorithms will require long-term follow-up data from the ongoing phase II and III clin. studies.

IT **220127-57-1**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; STI571 therapy and role of bcr-abl tyrosine kinase in chronic myelogenous leukemia in humans)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
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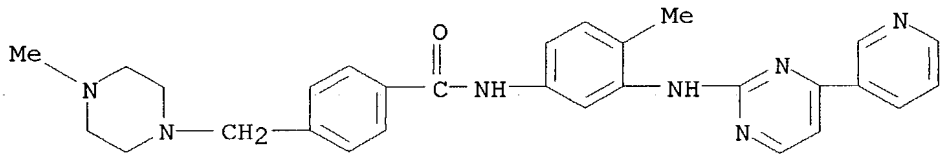
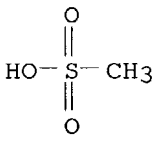


CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 97 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:379902 CAPLUS
DN 135:220870
TI Tyrosine kinase inhibitor STI571 potentiates the pharmacologic activity of retinoic acid in acute promyelocytic leukemia cells: effects on the degradation of RARα and PML-RARα
AU Gianni, Maurizio; Kalac, Yesim; Ponzanelli, Isabella; Rambaldi, Alessandro; Terao, Mineko; Garattini, Enrico
CS Divisione di Ematologia, Ospedali Riuniti di Bergamo, Bergamo, Italy
SO Blood (2001), 97(10), 3234-3243

CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB The 2-phenylaminopyrimidine derivative STI571 is a selective inhibitor of c-Abl, c-kit, and **platelet**-derived growth factor-receptor tyrosine kinases and is presently in phase II-III clin. studies. Here, this study reports on a novel pharmacol. activity of the compound, ie, enhancement of the cytodifferentiating, growth-inhibitory, and apoptogenic actions of all-trans-retinoic acid (ATRA). Whereas STI571 is not a cytodifferentiating agent by itself, the compound interacts with ATRA and enhances the myeloid maturation program set in motion by the retinoid in the PML-RARα+ acute promyelocytic leukemia NB4 and the PML-RARα- myeloblastic HL60 and U937 cell lines. In addition, STI571 relieves the cytodifferentiation block observed in the ATRA-resistant cell lines, NB4.R1, NB4.306, and NB4.007. In NB4 promyelocytes, a RARα agonist, but not an RXR agonist, can substitute for ATRA and interact with STI571. By contrast, STI571 is unique among c-Abl-specific tyrosine kinase inhibitors in modulating the pharmacol. activity of ATRA. In NB4 cells, enhanced cyto-differentiation results in increased up-regulation of the expression of a number of genes coding for myeloid differentiation markers, including CD11b, CD11c, and some of the components of the NADP-oxidase enzymic complex. All this is accompanied by inhibition of c-Abl tyrosine phosphorylation and retardation of the retinoid-dependent degradation of PML-RARα and RARα. Stabilization of the 2 retinoic acid receptors is likely to be the result of augmented and accelerated inhibition of the proteasome-dependent proteolytic activity observed on ATRA treatment.
IT **220127-57-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; tyrosine kinase inhibitor STI571 potentiates pharmacol. activity of retinoic acid in acute promyelocytic leukemia cells: effects on degradation of RARα and PML-RARα)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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CRN 152459-95-5
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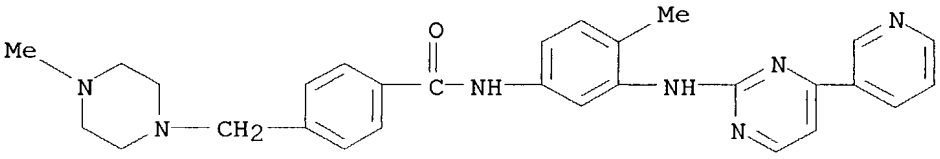
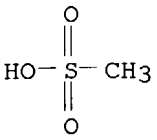


CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 98 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:301173 CAPLUS
DN 135:282774
TI Growth-inhibitory effect of STI571 on cells transformed by the COL1A1/PDGFB rearrangement
AU Greco, A.; Roccato, E.; Miranda, C.; Cleris, L.; Formelli, F.; Pierotti, M. A.
CS Department of Experimental Oncology, Operative Unit 3, Istituto Nazionale Tumori, Milan, 20133, Italy
SO International Journal of Cancer (2001), 92(3), 354-360
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Dermatofibrosarcoma protuberans (DP) is a skin tumor of intermediate malignancy characterized by high recurrence rates, for which surgical excision is the main therapy. All DP cases carry a specific t(17;22) translocation, resulting in a COL1A1/PDGFB rearrangement. The subsequently deregulated production of PDGFB generates autocrine stimulation of PDGFrβ, leading to malignant transformation. Using NIH-3T3 cells transformed by the COL1A1/PDGFB rearrangement (5A cell line), we explored the possibility of blocking the PDGFB autocrine loop, both in vitro and in vivo, using STI571, an inhibitor of the PDGF receptor and of ABL kinase activity. The presence of small amts. of serum in the culture medium was required for the in vitro growth and morphol. transformation of 5A cells. In the presence of STI571, the growth rate was reduced and the associated transformed phenotype changed to a flattened one. This effect could be reversed on removal of the inhibitor. The growth rate of tumors induced by 5A cells in nude mice was reduced by STI571 administration. Interestingly, this effect was also evident on pre-existing tumors, but no tumor eradication was observed This is consistent with the reversible effects of the inhibitor observed in vitro but differs from the eradication effect of STI571 on BCR-ABL-induced tumors. Our data indicate that STI571 might be a candidate compound for the pharmacol. treatment of DP and demonstrate that the same compound may act in different ways (cytotoxic vs. cytostatic), according to the specificity of the inhibited tyrosine kinase, namely, ABL or PDGFrβ.
IT **220127-57-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; STI571 growth-inhibitory effect on cells transformed by the COL1A1/PDGFB rearrangement)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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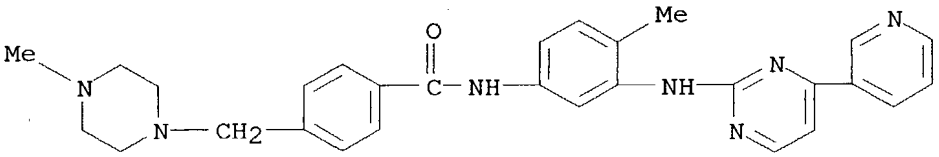
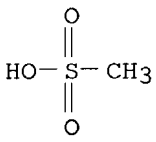


CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 99 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:297378 CAPLUS
DN 135:102132
TI ARG tyrosine kinase activity is inhibited by STI571
AU Okuda, Keiko; Weisberg, Ellen; Gilliland, D. Gary; Griffin, James D.
CS Department of Adult Oncology, Dana Farber Cancer Institute, Boston, MA, 02115, USA
SO Blood (2001), 97(8), 2440-2448
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB The tyrosine kinase inhibitor STI571 inhibits BCR/ABL and induces hematol. remission in most patients with chronic myeloid leukemia. In addition to BCR/ABL, STI571 also inhibits v-Abl, TEL/ABL, the native **platelet**-derived growth factor (PDGF)β receptor, and c-KIT, but it does not inhibit SRC family kinases, c-FMS, FLT3, the epidermal growth factor receptor, or multiple other tyrosine kinases. ARG is a widely expressed tyrosine kinase that shares substantial sequence identity with c-ABL in the kinase domain and cooperates with ABL to regulate neurulation in the developing mouse embryo. As described here, ARG has recently been implicated in the pathogenesis of leukemia as a fusion partner of TEL. A TEL/ARG fusion was constructed to determine whether ARG can be inhibited by STI571. When expressed in the factor-dependent murine hematopoietic cell line Ba/F3, the TEL/ARG protein was heavily phosphorylated on tyrosine, increased tyrosine phosphorylation of multiple cellular proteins, and induced factor-independent proliferation. The effects of STI571 on Ba/F3

cells transformed with BCR/ABL, TEL/ABL, TEL/PDGFβR, or TEL/ARG were then compared. STI571 inhibited tyrosine phosphorylation and cell growth of Ba/F3 cells expressing BCR/ABL, TEL/ABL, TEL/PDGFβR, and TEL/ARG with an IC50 of approx. 0.5 μM in each case, but it had no effect on untransformed Ba/F3 cells growing in IL-3 or on Ba/F3 cells transformed by TEL/JAK2. Culture of TEL/ARG-transfected Ba/F3 cells with IL-3 completely prevented STI571-induced apoptosis in these cells, similar to what has been observed with BCR/ABL- or TEL/ABL-transformed cells. These results indicate that ARG is a target of the small mol., tyrosine kinase inhibitor STI571.

IT **220127-57-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(STI 571; ARG tyrosine kinase inhibition by STI571)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
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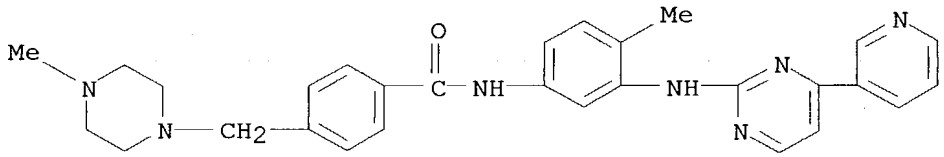
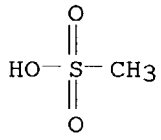


CM 2

CRN 75-75-2
CMF C H4 O3 S



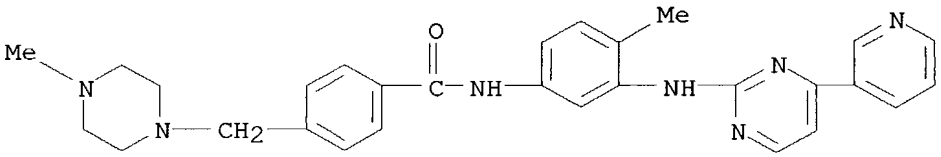
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 100 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:295904 CAPLUS
DN 135:102120
TI Inhibition of **platelet**-derived growth factor receptors reduces interstitial hypertension and increases transcapillary transport in tumors
AU Pietras, Kristian; Ostman, Arne; Sjoquist, Mats; Buchdunger, Elisabeth; Reed, Rolf K.; Heldin, Carl-Henrik; Rubin, Kristofer
CS Ludwig Institute for Cancer Research, Uppsala, SE-751 24, Swed.
SO Cancer Research (2001), 61(7), 2929-2934

CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Most solid malignancies display interstitial hypertension and a poor uptake of anticancer drugs. **Platelet**-derived growth factor (PDGF) and the cognate tyrosine kinase receptors are expressed in many tumors. Signaling through PDGFβ receptors was shown recently to increase interstitial fluid pressure (IFP) in dermis after anaphylaxis-induced lowering of IFP. In this study, we show that treatment with the selective PDGF receptor kinase inhibitor, ST 1571, formerly known as CGP57148B, decreased the interstitial hypertension and increased capillary-to-interstitium transport of 51Cr-EDTA in s.c. growing rat PROb colonic carcinomas. Furthermore, treatment with an antagonistic PDGF-B oligonucleotide aptamer decreased interstitial hypertension in these tumors. PDGFβ receptors were expressed in blood vessels and stromal cells but not in the tumor cells of PROb colonic carcinomas. Our study indicates a previously unrecognized role of PDGF receptors in tumor biol., although similar effects of PDGF on IFP have been demonstrated previously in the dermis. The data suggest interference with PDGF receptors, or their ligands, as a novel strategy to increase drug uptake and therapeutic effectiveness of cancer chemotherapy.
IT **220127-57-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; inhibition of **platelet**-derived growth factor receptors reduces interstitial hypertension and increases transcapillary transport in tumors)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

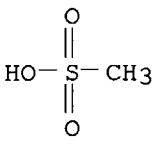
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

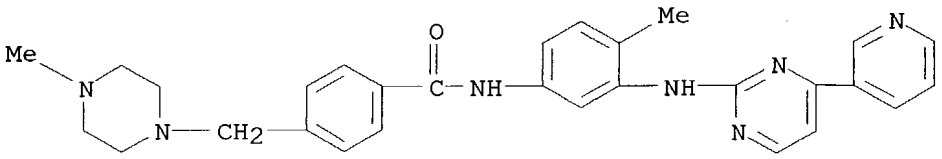


RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 101 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:286847 CAPLUS
DN 135:204687
TI Overview: recent success with the tyrosine kinase inhibitor STI-571 - lessons for targeted therapy of cancer
AU Shah, Neil P.; Sawyers, Charles L.
CS Department of Medicine, University of California Los Angeles, Los Angeles, CA, 90095-1678, USA
SO Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2001), 2(3), 422-423
CODEN: COIDAZ
PB PharmaPress Ltd.
DT Journal; General Review
LA English
AB A review with 17 refs. Chronic myelogenous leukemia (CML) provides an instructive example of a disease for which target-based therapy has recently made an elegant transition from the mol. biol. laboratory to the clinic. Nearly all cases of CML are associated with a specific genetic alteration, known as the Philadelphia chromosome. The human genome is anticipated to harbor -150 different tyrosine kinases. Many are involved in growth-factor signal transduction and oncogenesis, as demonstrated by their frequent isolation from animal tumor viruses. Therefore, inhibitors of tyrosine kinases would be expected to have antitumor activity. One such compound, STI-571 (Novartis AG), a 2-phenylaminopyrimidine, preferentially inhibited Bcr-Abl, as well as **platelet**-derived growth factor receptor (PDGFR) and the hematopoietic stem cell receptor, Kit. It can be argued that CML, by nature of its reliance upon a single genetic mutation in nearly all cases, may represent the ideal disease in which targeted therapy might be expected to produce a clin. response. It is important to reiterate that STI-571 has efficacy even in the advanced phases of CML, when numerous growth-regulatory mutations have occurred in addition to the Philadelphia chromosome translocation. Thus, the initiating oncogenic event in a cancer remains critical for maintenance of the cancer, even at its late, most genetically complex stages. Given the ongoing commitment of several drug companies to the development of specific mol. pathway inhibitors, it is likely that the next decade will yield a panel of STI-like drugs with specificity for different pathways. The challenge, of course,. lies in choosing the correct inhibitor for a particular cancer. Other technologies, such as proteomics, are also in development and may play a role as well.
IT **220127-57-1**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; tyrosine kinase inhibitor STI-571 for therapy of cancer in humans)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

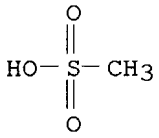
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 102 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:285596 CAPLUS
DN 135:220387
TI Mechanisms of resistance to imatinib (STI 571) and prospects for combination with conventional chemotherapeutic agents
AU Krystal, Geoffrey W.
CS Department of Medicine, Medical College of Virginia of Virginia Commonwealth University, Richmond, VA, USA
SO Drug Resistance Updates (2001), 4(1), 16-21
CODEN: DRUPFW; ISSN: 1368-7646
PB Harcourt Publishers Ltd.
DT Journal; General Review
LA English
AB A review with 36 refs. is given. Imatinib (STI 571, Glivec) is a small mol. drug selected for its ability to inhibit the Bcr-Abl kinase, the pathogenic mol. abnormality in chronic myelogenous leukemia (CML). It also is an efficient inhibitor of the Kit and **platelet**-derived growth factor receptor tyrosine kinases. In vitro studies have demonstrated that this drug potently inhibits proliferation and induces apoptosis of cells that depend on activation of these kinases. Phase I clin. studies have demonstrated remarkable activity against CML. However, these studies, as well as a variety of exptl. models, have suggested that clin. resistance to STI 571 could develop. The mechanisms for the development of this resistance will be discussed along with the potential for circumventing STI 571 resistance by combining it with traditional anti-neoplastic agents.
IT **220127-57-1**, Imatinib mesylate
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or

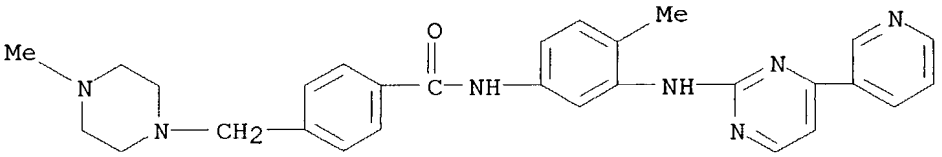
effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(resistance to STI 571)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

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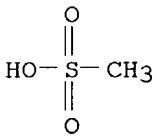
CMF C H4 O3 S



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 103 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:728380 CAPLUS

DN 134:491

TI Abl protein-tyrosine kinase inhibitor STI571 inhibits in vitro signal transduction mediated by c-Kit and **platelet**-derived growth factor receptors

AU Buchdunger, Elisabeth; Cioffi, Catherine L.; Law, Norman; Stover, David; Ohno-Jones, Sayuri; Druker, Brian J.; Lydon, Nicholas B.

CS Novartis Pharma AG, Oncology Research, Basel, CH-4002, Switz.

SO Journal of Pharmacology and Experimental Therapeutics (2000), 295(1), 139-145
CODEN: JPETAB; ISSN: 0022-3565

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

AB STI571 (formerly known as CGP 57148B) is a protein-tyrosine kinase inhibitor that is currently in clin. trials for the treatment of chronic myelogenous leukemia. STI571 selectively inhibits the Abl and **platelet**-derived growth factor (PDGF) receptor tyrosine kinases in vitro and blocks cellular proliferation and tumor growth of Bcr-abl- or

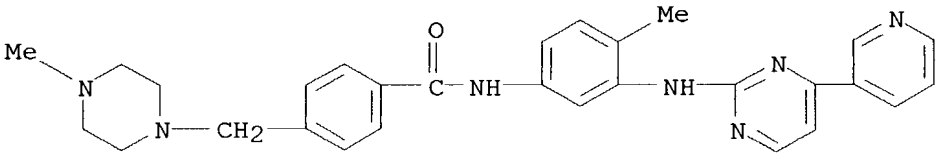
v-abl-expressing cells. We have further investigated the profile of STI571 against related receptor tyrosine kinases. STI571 was found to potently inhibit the kinase activity of the α- and β-PDGF receptors and the receptor for stem cell factor, but not the closely related c-Fms, Flt-3, Kdr, Flt-1, and Tek tyrosine kinases. Addnl., no inhibition of c-Met or nonreceptor tyrosine kinases such as Src and Jak-2 has been observed In cell-based assays, STI571 selectively inhibited PDGF and stem cell factor-mediated cellular signaling, including ligand-stimulated receptor autophosphorylation, inositol phosphate formation, and mitogen-activated protein kinase activation and proliferation. These results expand the profile of STI571 and suggest that in addition to chronic myelogenous leukemia, STI571 may have clin. potential in the treatment of diseases that involve abnormal activation of c-Kit or PDGF receptor tyrosine kinases.

IT **220127-57-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; abl protein-tyrosine kinase inhibitor STI571 inhibits in vitro signal transduction mediated by c-Kit and **platelet** -derived growth factor receptors)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

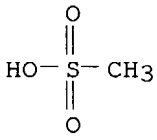
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



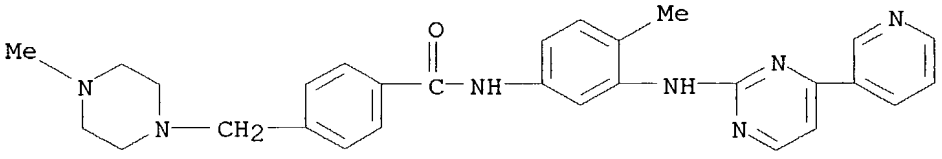
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 104 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:702580 CAPLUS

DN 134:271
TI Intracranial inhibition of **platelet**-derived growth factor-mediated glioblastoma cell growth by an orally active kinase inhibitor of the 2-phenylaminopyrimidine class
AU Kilic, Turker; Alberta, John A.; Zdunek, Pawel R.; Acar, Melih; Iannarelli, Palma; O'Reilly, Terence; Buchdunger, Elisabeth; Black, Peter M.; Stiles, Charles D.
CS Neurosurgical Laboratories and Brain Tumor Center and Department of Surgery, Harvard Medical School, Brigham and Women's Hospital, The Children's Hospital, Boston, MA, 02115, USA
SO Cancer Research (2000), 60(18), 5143-5150
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Glioblastoma multiforme is the most common primary human brain tumor, and it is, for all practical purposes, incurable in adult patients. The high mortality rates reflect the fact that glioblastomas are resistant to adjuvant therapies (radiation and chems.), the mode of action of which is cytotoxic. We show here that an p.o.-active small mol. kinase inhibitor of the 2-phenylaminopyrimidine class may have therapeutic potential for glioblastomas. STI571 inhibits the growth of U343 and U87 human glioblastoma cells that have been injected into the brains of nude mice, but it does not inhibit intracranial growth of ras-transformed cells. Studies on a broad panel of genetically validated human and animal cell lines show that STI571 acts by disruption of the ligand:receptor autocrine loops for **platelet**-derived growth factor that are a pervasive feature of malignant astrocytoma. The cellular response of glioblastoma cells to STI571 does not appear to involve an apoptotic mechanism.
IT **220127-57-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; intracranial inhibition of PDGF-mediated glioblastoma by an orally active inhibitor of phenylaminopyrimidine class)
RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

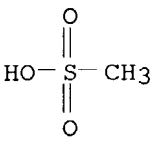
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



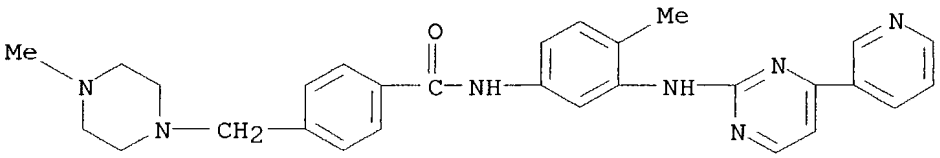
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 105 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:647564 CAPLUS
DN 134:125648
TI The selective tyrosine kinase inhibitor STI571 inhibits small cell lung cancer growth
AU Krystal, Geoffrey W.; Honsawek, Sittisak; Litz, Julie; Buchdunger, Elisabeth
CS Department of Medicine, Division of Hematology/Oncology and Department of Microbiology/Immunology McGuire, Virginia Commonwealth University, Richmond, VA, 23249, USA
SO Clinical Cancer Research (2000), 6(8), 3319-3326
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB At least 70% of small cell lung cancers express the Kit receptor Tyr kinase and its ligand, stem cell factor (SCF). Numerous lines of evidence have demonstrated that this coexpression constitutes a functional autocrine loop, suggesting that inhibitors of Kit Tyr kinase activity could have therapeutic efficacy in this disease. STI571, formerly known as CGP 57148B, is a p.o. bioavailable 2-phenylaminopyrimide derivative that was designed as an Abl Tyr kinase inhibitor, but also has efficacy against the **platelet**-derived growth factor receptor and Kit in vitro. Pretreatment of the H526 small cell lung cancer (SCLC) cell line with STI571 inhibited SCF-mediated Kit activation with an IC50 of 0.1 μM as measured by inhibition of receptor Tyr phosphorylation and 0.2 μM as measured by immune complex kinase assay. Tis paralleled the inhibition of SCF-mediated growth by STI571, which had an IC50 of .apprx.0.3 μM. Growth inhibition in SCF-containing medium was accompanied by induction of apoptosis. STI571 efficiently blocked SCF-mediated activation of mitogen-activated protein kinase and Akt, but did not affect insulin-like growth factor-1 or serum-mediated mitogen-activated protein kinase or Akt activation. Growth of 5 of 6 SCLC cell lines in medium containing 10% FCS was inhibited by STI571 with an IC50 of .apprx.5 μM. Growth inhibition in serum-containing medium appeared to be cytostatic in nature because no increase in apoptosis was observed Despite this growth inhibition, STI571 failed to enhance the cytotoxicity of either carboplatinum or etoposide when coadministered. However, taken together with the minimal toxicity that this compound has shown in preclin. studies, these data suggest that STI571 could have a role in the treatment of SCLC, possibly to block or slow recurrence after chemotherapy-induced remissions.
IT **220127-57-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(STI 571; STI571 inhibited small cell lung cancer growth)
RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

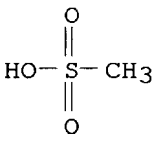
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 106 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:536162 CAPLUS
DN 133:217392
TI Inhibition of c-kit receptor tyrosine kinase activity by STI 571, a selective tyrosine kinase inhibitor
AU Heinrich, Michael C.; Griffith, Diana J.; Druker, Brian J.; Wait, Cecily L.; Ott, Kristen A.; Zigler, Amy J.
CS Division of Hematology and Medical Oncology, Department of Medicine, Portland Veterans Affairs Medical Center, Oregon Health Sciences University, Portland, OR, USA
SO Blood (2000), 96(3), 925-932
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB STI 571 (formerly known as CGP 57148B) is a known inhibitor of the c-abl, bcr-abl, and **platelet**-derived growth-factor receptor (PDGFR) tyrosine kinases. This compound is being evaluated in clin. trials for the treatment of chronic myelogenous leukemia. We sought to extend the activity profile of STI 571 by testing its ability to inhibit the tyrosine kinase activity of c-kit, a receptor structurally similar to PDGFR. We treated a c-kit expressing a human myeloid leukemia cell line, M-07e, with STI 571 before stimulation with Steel factor (SLF). STI 571 inhibited c-kit autophosphorylation, activation of mitogen-activated protein (MAP)

kinase, and activation of Akt without altering total protein levels of c-kit, MAP kinase, or Akt. The concentration that produced 50% inhibition for these effects was approx. 100 nmol/L. STI 571 also significantly decreased SLF-dependent growth of M-07e cells in a dose-dependent manner and blocked the antiapoptotic activity of SLF. In contrast, the compound had no effect on MAP kinase activation or cellular proliferation in response to granulocyte-macrophage colony-stimulating factor. We also tested the activity of STI 571 in a human mast cell leukemia cell line (HMC-1), which has an activated mutant form of c-kit. STI 571 had a more potent inhibitory effect on the kinase activity of this mutant receptor than it did on ligand-dependent activation of the wild-type receptor. These findings show that STI 571 selectively inhibits c-kit tyrosine kinase activity and downstream activation of target proteins involved in cellular proliferation and survival. This compound may be useful in treating cancers associated with increased c-kit kinase activity.

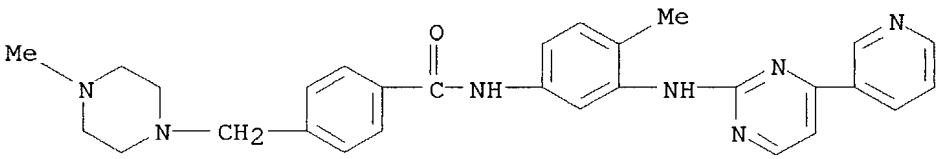
IT **220127-57-1**, STI 571
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of c-kit receptor tyrosine kinase activity by STI 571, a selective tyrosine kinase inhibitor)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

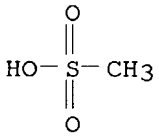
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



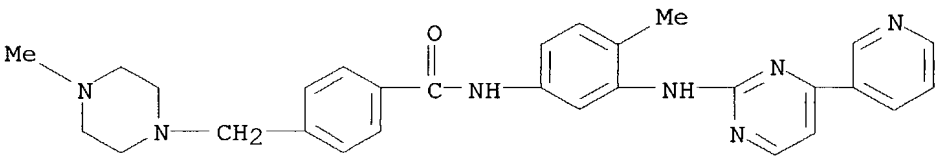
RE.CNT 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l18 1-35 fbib ab hitstr

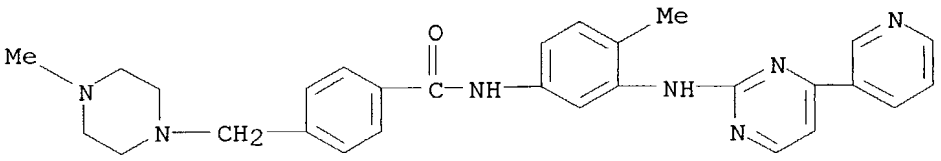
L18 ANSWER 1 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:331787 CAPLUS
TI Treatment of tuberous sclerosis associated neoplasms with **platelet** -derived growth factor receptor tyrosine kinase or bcr-abl tyrosine kinase inhibitors, especially N-phenyl-2-pyrimidineamines
IN Arbiser, Jack
PA USA
SO U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004077661	A1	20040422	US 2003-655407	20030904
			US 2002-408550PP	20020905

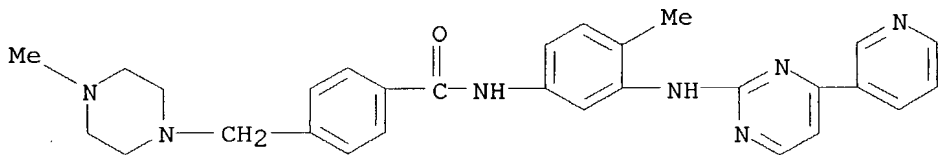
AB The present invention relates to the use of PDGF receptor tyrosine kinase or bcr-abl tyrosine kinase inhibitors, especially of N-phenyl-2-pyrimidine-amine derivs. I (R1 = 4-pyrazinyl, 1-methyl-1H-pyrrolyl, etc.; R2, R3 = H, lower alkyl; R4-8 = nitro, fluoro-substituted lower alkoxy, -N(R9)-C(=X)-(Y)nR10; R9 = H, lower alkyl; X = oxo, thio, imino, N-lower alkylimino, hydroximino, or O-lower alkyl-hydroximino; Y = O, NH; n = 0 or 1; R10 = C5 aliphatic radical, aromatic, etc.) or in pharmaceutically acceptable salt form, in the manufacture of a pharmaceutical composition for the treatment of tuberous sclerosis associated neoplasms; to a method of treatment of warm-blooded animals, including humans, suffering from a tuberous sclerosis associated neoplasms. Cells of SV7tert, a cell line derived from a human angiomyolipoma, were inhibited by 4-(4-methyl-1-piperazin-1-ylmethyl)-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]benzamide.
IT **152459-95-5 152459-95-5D**, acceptable salts
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tuberous sclerosis-associated neoplasms treatment with **platelet** -derived growth factor receptor tyrosine kinase or bcr-abl tyrosine kinase inhibitors, especially N-Ph-2-pyrimidineamines)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



L18 ANSWER 2 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:309651 CAPLUS
DN 140:336909
TI NIN, a Gene Encoding a CEP110-Like Centrosomal Protein, Is Fused to PDGFRB in a Patient with a t(5;14)(q33;q24) and an Imatinib-Responsive Myeloproliferative Disorder
AU Vizmanos, Jose L.; Novo, Francisco J.; Roman, Jose P.; Baxter, E. Joanna; Lahortiga, Idoya; Larrayoz, Maria J.; Odero, Maria D.; Giraldo, Pilar; Calasanz, Maria J.; Cross, Nicholas C. P.
CS Department of Genetics, University of Navarra, Pamplona, E-31008, Spain
SO Cancer Research (2004), 64(8), 2673-2676
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB The authors describe a new PDGFRB fusion associated with a t(5;14)(q33;q24) in a patient with a longstanding chronic myeloproliferative disorder with eosinophilia. After confirmation of PDGFRB involvement and definition of the chromosome 14 breakpoint by fluorescence in situ hybridization, candidate partner genes were selected on the basis of the presence of predicted oligomerization domains believed to be an essential feature of tyrosine kinase fusion proteins. The authors demonstrate that the t(5;14) fuses PDGFRB to NIN, a gene encoding a centrosomal protein with CEP110-like function. After treatment with imatinib, the patient achieved hematol. and cytogenetical remission, but NIN-PDGFRB mRNA remained detectable by reverse transcription-PCR.
IT **152459-95-5**, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NIN, gene encoding CEP110-like centrosomal protein, is fused to PDGFRB in patient with t(5;14)(q33;q24) and an imatinib-responsive myeloproliferative disorder with eosinophilia)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:100803 CAPLUS

DN 140:139483
TI Method for enhancing the effectiveness of therapies of hyperproliferative diseases
IN Chang, Yan; Sasak, Vodek
PA USA
SO U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 176,235.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

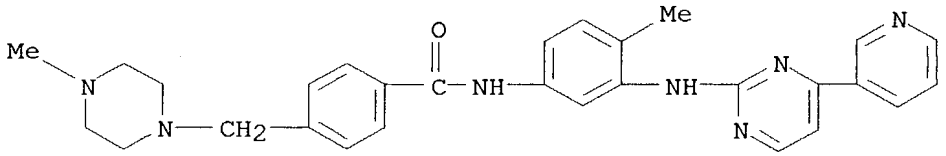
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004023925	A1	20040205	US 2003-408723	20030407
				US 2001-299991PP	20010621
				US 2002-176235 A2	20020620
	US 2003013681	A1	20030116	US 2002-176235	20020620
	US 6680306	B2	20040120		
				US 2001-299991PP	20010621
	US 2004043962	A1	20040304	US 2003-657383	20030908
				US 2001-299991PP	20010621
				US 2002-176235 A1	20020620

PATENT FAMILY INFORMATION:
FAN 2003:5701

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003000118	A2	20030103	WO 2002-US19885	20020621
	WO 2003000118	A3	20030410		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
				US 2001-299991PP	20010621
				US 2002-176235 A	20020620
	US 2003013681	A1	20030116	US 2002-176235	20020620
	US 6680306	B2	20040120		
				US 2001-299991PP	20010621
	EP 1406639	A2	20040414	EP 2002-749641	20020621
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
				US 2001-299991PP	20010621
				US 2002-176235 A	20020620
				WO 2002-US19885W	20020621
	US 2004043962	A1	20040304	US 2003-657383	20030908
				US 2001-299991PP	20010621
				US 2002-176235 A1	20020620

AB The efficacy of conventional cancer therapies such as surgery, chemotherapy and radiation is enhanced by the use of a therapeutic material which binds to and interacts with galectins. The therapeutic material can enhance apoptosis thereby increasing the effectiveness of oncolytic agents. It can also inhibit angiogenesis thereby moderating tumor growth and/or metastasis.
IT **152459-95-5**, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(method for enhancing effectiveness of therapies of hyperproliferative diseases)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



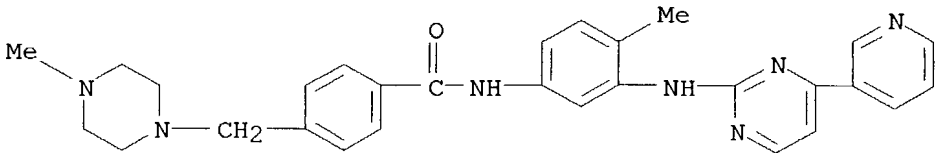
L18 ANSWER 4 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:41213 CAPLUS
DN 140:105249
TI Combination of mTOR inhibitor and a tyrosine kinase inhibitor for the treatment of neoplasms
IN Neel, Benjamin G.; Mohi, Golam
PA Beth Israel Deaconess Medical Center, USA
SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004004644	A2	20040115	WO 2003-US20972	20030703

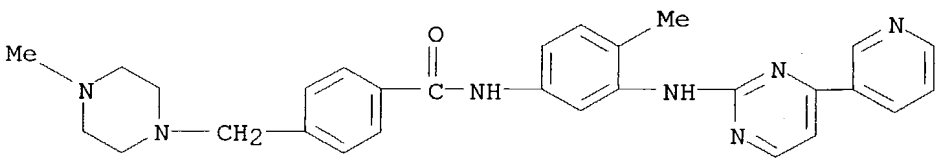
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-394029PP 20020705
US 2002-412402PP 20020920

AB The invention features methods and compns. including an mTOR inhibitor and a tyrosine kinase inhibitor for reducing the proliferation of and enhancing the apoptosis of neoplastic cells. The addition of an MEK inhibitor to this combination further enhances the effectiveness of this therapeutic method.
IT **152459-95-5**, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of mTOR inhibitor and tyrosine kinase inhibitor for cancer therapy)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



L18 ANSWER 5 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:952624 CAPLUS
DN 140:109132
TI Cloning of the t(1;5)(q23;q33) in a myeloproliferative disorder associated with eosinophilia: Involvement of PDGFRB and response to imatinib
AU Wilkinson, Kathryn; Velloso, Elvira R. P.; Lopes, Luiz Fernando; Lee, Charles; Aster, Jon C.; Shipp, Margaret A.; Aguiar, Ricardo C. T.
CS Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA, USA
SO Blood (2003), 102(12), 4187-4190
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Eosinophilia is common in myeloproliferative disorders (MPDs) with abnormalities of chromosome band 5q31-33, including those that present with t(1;5)(q23;q33). With the development of rational drug therapy, characterization of the mol. targets for these translocations could guide treatment and affect patient survival. We cloned the t(1;5)(q23;q33) and showed that it fuses **platelet**-derived growth factor receptor beta (PDGFRB) to the coiled-coil domains of a novel partner protein, myomegalin. Using two-color interphase fluorescence in situ hybridization (FISH), we also demonstrated that the eosinophils are clonal in these disorders. Imatinib mesylate has recently been shown to be efficacious in MPDs with PDGFR activation. Therefore, following our mol. studies, we were able to redirect this patient's treatment. Although she had refractory and progressive disease, once imatinib was started, complete clin. and hematol. remission, as well as major cytogenetic response, was achieved. Given the therapeutic implications, our findings stress the need to aggressively investigate the mol. basis of these diseases, with emphasis on the PDGFR family.
IT **152459-95-5**, Imatinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cloning of t(1;5)(q23;q33) in a myeloproliferative disorder associated with eosinophilia and involvement of PDGFRB and response to imatinib in human)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:912990 CAPLUS
DN 139:375014
TI Methods and compositions with N-phenyl-2-pyrimidine compounds inhibiting **platelet** derived growth factor receptor for the treatment of graft failure
IN Sukhatme, Vikas P.
PA Beth Israel Deaconess Medical Center, USA
SO PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

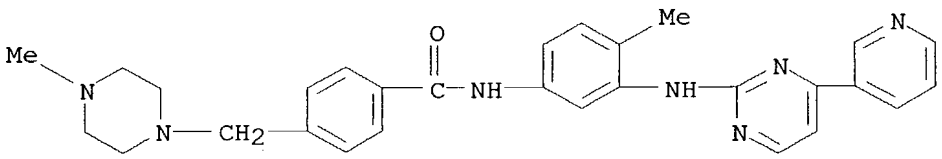
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003094904	A1	20031120	WO 2003-US14916	20030513

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-380180PP 20020513
US 2003-464023PP 20030418

OS MARPAT 139:375014
AB The present invention provides methods and compns. for treating graft failure resulting from neointimal hyperplasia. These methods and compns. feature the use of **platelet** derived growth factor receptor (PDGFR) inhibitor compds., such as N-phenyl-2-pyrimidine compds. (e.g., imatinib mesylate) to inhibit the biol. activity of the PDGFR and treat AV graft failure. Gleevec and rapamycin inhibited smooth muscle cell migration.
IT **152459-95-5**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-Ph-2-pyrimidine compds. inhibiting **platelet** derived growth factor receptor for treatment of graft failure)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



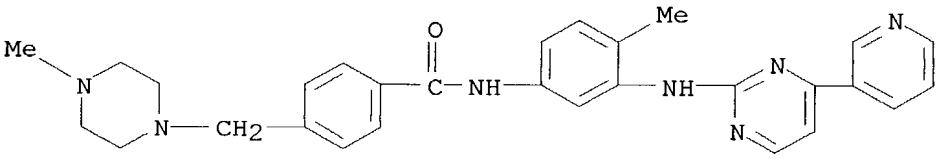
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:875113 CAPLUS
DN 139:345924
TI PDGF receptor tyrosine kinase inhibitors for the treatment of polycythemia vera
IN Kantarjian, Hagop
PA Board of Regents, the University of Texas System, USA
SO PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003090750	A1	20031106	WO 2003-IB1632	20030422

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR
US 2002-375143PP 20020424

AB The invention discloses the treatment of polycythemia vera by administration of N-[5-(4-(4-methylpiperazinomethyl)benzoylamido)-2-methylphenyl]-4-(3-pyridyl)-2-pyrimidineamine or 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-((4-(3-pyridinyl)-2-pyrimidinyl)amino)phenyl]benzamide in free form or in pharmaceutically acceptable salt form.
IT **152459-95-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PDGF receptor tyrosine kinase inhibitors for treatment of polycythemia vera)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:757504 CAPLUS
DN 139:271054
TI Imatinib for treating angiotensin II-mediated diseases
IN Gilbert, Richard Ernest; Kelly, Darren James; Feldman, David Louis
PA Novartis A.-G., Switz.; The University of Melbourne
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003077892	A2	20030925	WO 2003-EP2709	20030314
	WO 2003077892	A3	20031224		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

GB 2002-6216 A 20020315
GB 2002-6217 A 20020315
GB 2002-17505 A 20020729

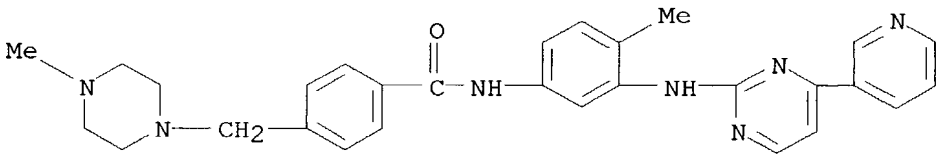
OS MARPAT 139:271054

AB A PDGF receptor tyrosine kinase inhibitor, especially 4-(4-methylpiperazin-1-ylmethyl)-N-[[4-methyl-3-(4-pyridin-3-yl)pyrimidin-2-ylamino]phenyl]benzamide (I) or a pharmaceutically acceptable salt can be used in the treatment of angiotensin II-induced diseases and a combination which comprises (a) a PDGF receptor tyrosine kinase inhibitor, an antihypertensive, an aldosterone antagonist, an aldosterone synthase inhibitor and/or an angiotensin receptor blocker agent and optionally at least one pharmaceutically acceptable carrier for simultaneous, sep. or sequential use, in particular for the treatment of hypertension and hypertension-induced diseases. Imatini9b had no effect on systolic blood pressure but significantly reduced mesenteric weight in animals receiving angiotensin II. Pharmaceutical formulations of Imatinib were given.

IT **152459-95-5**, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Imatinib for treating angiotensin II-mediated diseases)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



L18 ANSWER 9 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:714202 CAPLUS

DN 140:192344

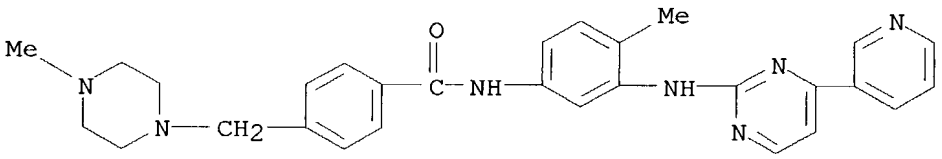
TI Imatinib inhibits the in vitro development of the monocyte/macrophage lineage from normal human bone marrow progenitors

AU Dewar, A. L.; Domaschenz, R. M.; Doherty, K. V.; Hughes, T. P.; Lyons, A. B.

CS Hanson Institute, Division of Haematology, Institute of Medical and Veterinary Science, Adelaide, Australia

SO Leukemia (2003), 17(9), 1713-1721

CODEN: LEUKED; ISSN: 0887-6924
PB Nature Publishing Group
DT Journal
LA English
AB The antileukemic tyrosine kinase inhibitor, imatinib, has been reported to inhibit specifically the growth of bcr-abl expressing CML progenitors at levels of 0.1-5.0 μM, by blocking the ATP-binding site of the kinase domain of bcr-abl. Inhibition of the c-abl, **platelet**-derived growth factor receptor and stem cell factor receptor (c-kit) tyrosine kinases by imatinib has also been reported. Here, we demonstrate that imatinib significantly inhibits in vitro monocyte/macrophage development from normal bone marrow progenitors, while neutrophil and eosinophil development was less affected. Monocyte/macrophage inhibition was observed in semisolid agar and liquid cultures at concns. of imatinib as low as 0.3 μM. The maturation of monocytes into macrophages was also found to be impaired following treatment of cultures with 1.0 μM imatinib. Imatinib blocked monocyte/macrophage development in cultures stimulated with and without M-CSF, suggesting that inhibition of the M-CSF receptor, c-fms, by imatinib was unlikely to be responsible. Imatinib may therefore have an inhibitory activity for other kinase(s) that play a role in monocyte/macrophage differentiation. This inhibition of normal monocyte/macrophage development was observed at concns. of imatinib achievable pharmacol., suggesting that imatinib or closely related derivs. may have potential for the treatment of diseases where monocytes/macrophages contribute to pathogenesis.
IT **152459-95-5**, Imatinib
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib inhibits the in vitro development of monocyte/macrophage lineage from normal human bone marrow progenitors)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:696780 CAPLUS
DN 139:219397
TI N-{5-[4-(4-methyl-piperazino-methyl)-benzoylamido]-2-methylphenyl}-4-(3-pyridyl)-2-pyrimidine-amine coated stents
IN Prescott, Margaret Forney; Feldman, David Louis
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 2003072159	A1	20030904	WO 2003-EP2028	20030227

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR

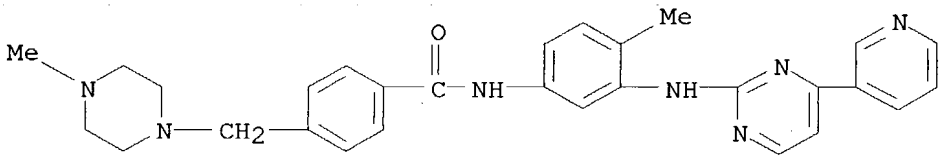
US 2002-360254PP 20020228

AB The invention relates to the local administration of N-{5-[4-(4-methyl-piperazino-methyl)-benzoylamido]-2-methylphenyl}-4-(3-pyridyl)-2-pyrimidine-amine (I) or a pharmaceutically acceptable salt or crystal form thereof, optionally in conjunction with one or more other active ingredients, and a device adapted for such local administration. I significantly reduced neointimal lesion formation in rats at 28 days following balloon injury when administered at a dose of 0.2-3.5 mg/kg.

IT **152459-95-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(piperazino-methylbenzoylamido pyridylpyrimidineamine coated stents)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:696725 CAPLUS
DN 139:207735
TI Use of tyrosine kinase inhibitors for treating CNS disorders
IN Moussy, Alain; Kinet, Jean-Pierre
PA AB Science, Fr.
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003072090	A2	20030904	WO 2003-IB1425	20030226
	WO 2003072090	A3	20031113		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,

RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002-359652PP 20020227

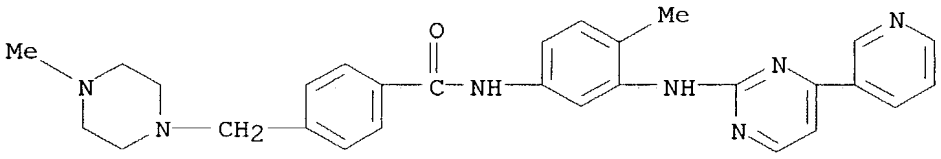
OS MARPAT 139:207735

AB The present invention relates to a method for treating CNS disorders, more particularly selected from the group consisting of depression, schizophrenia, anxiety, migraine, memory loss, pain and neurodegenerative diseases, comprising administering a compound capable of depleting mast cells to a human in need of such treatment. Such compds. can be chosen from tyrosine kinase inhibitors and more particularly non-toxic, selective and potent c-kit inhibitors. Preferably, said inhibitor is unable to promote death of IL-3 dependent cells cultured in presence of IL-3.

IT **152459-95-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tyrosine kinase inhibitors for treating CNS disorders)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



L18 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:656611 CAPLUS

DN 139:191397

TI Tissue growth factor receptor inhibitor combinations for treating hyperproliferative conditions

IN Stiles, Charles Dean

PA Dana-Farber Cancer Institute, Inc., USA; Novartis A.-G.

SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003068265	A1	20030821	WO 2003-EP1507	20030214

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR
US 2002-356912PP 20020214

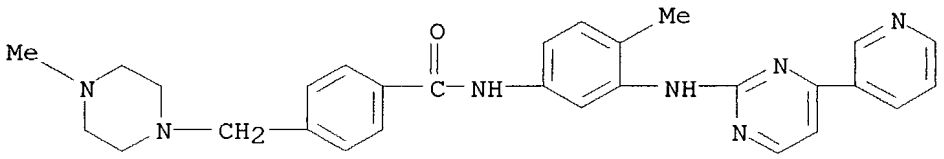
AB The present invention relates to a combination which comprises (a) an inhibitor of a tissue non-specific growth factor receptor and (b) an

inhibitor of a tissue specific growth factor receptor for simultaneous, concurrent, sep. or sequential use, especially for use in the treatment of hyperproliferative conditions, such as in particular cancer, in a mammal, particularly a human. An example is given showing the synergistic effect on cell growth of combined inhibition of **platelet**-derived growth factor receptor signalling and insulin-like growth factor signalling using the small mol. signal transduction inhibitors STI-571 (I) and ADW (II).

IT **152459-95-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tissue growth factor receptor inhibitor combinations for treating hyperproliferative conditions)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

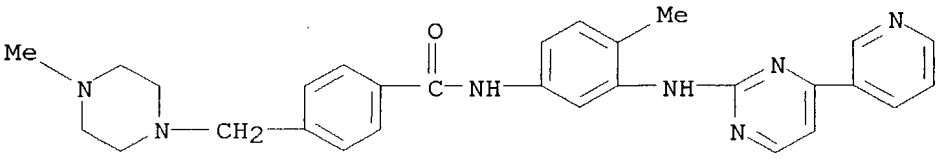
L18 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:639686 CAPLUS
DN 140:139030
TI Leflunomide analogue FK778 is vasculoprotective independent of its immunosuppressive effect: potential applications for restenosis and chronic rejection
AU Savikko, Johanna; von Willebrand, Eva; Haeyry, Pekka
CS Transplantation Laboratory, Haartman Institute, Helsinki Univ. Central Hospital, Helsinki, Finland
SO Transplantation (2003), 76(3), 455-458
CODEN: TRPLAU; ISSN: 0041-1337
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB BACKGROUND: Leflunomide (LFM) inhibits exptl. both acute and chronic allograft rejection. The inhibition of dihydroorotate dehydrogenase (DHODH) in pyrimidine synthesis is suggested to be the major immunosuppressive mechanism. The mechanism of its vasculoprotective effect is not known, although it may be linked to inhibition of receptor tyrosine kinases (RTK). Here, we have investigated whether sufficient vasculoprotective effect could be obtained upon administration of FK778, a LFM analog with shorter half-life, and compared the dose response with that of a known **platelet**-derived growth factor RTK inhibitor, imatinib, after endothelial injury in vivo. METHODS AND RESULTS: Wistar rats were used for aorta denudations. The rats remained untreated or received either FK778 or imatinib (STI571) at decreasing oral doses from 10 mg/kg per day. Half of the animals in both treatment groups also received uridine to reverse DHODH activity. Morphometric anal. was done after 14 day follow-up. In the untreated group, moderate neointima formation was detected. FK778 almost completely inhibited intimal formation, with or without uridine addition ($P<0.05$). Imatinib also

inhibited neointima formation (P<0.05), whereas exogenous uridine reversed its effect. CONCLUSIONS: Our results demonstrate that FK778 inhibits neointima formation by way of a mechanism that is independent of DHODH inhibitory activity on vascular smooth muscle cell. Interestingly, the effect of imatinib was inhibited by uridine, suggesting that part of its action on vascular stenosis could be mediated through inhibition of pyrimidine synthesis.

IT **152459-95-5**, Imatinib
RL: PAC (Pharmacological activity); BIOL (Biological study)
(leflunomide analog FK778 is vasculoprotective independent of its immunosuppressive effect in relation to imatinib)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:638789 CAPLUS

DN 139:228345

TI An activated receptor tyrosine kinase, TEL/PDGFβR, cooperates with AML1/ETO to induce acute myeloid leukemia in mice

AU Grisolano, Jay L.; O'Neal, Julie; Cain, Jennifer; Tomasson, Michael H.

CS Departments of Medicine and Genetics, Division of Oncology, Siteman Cancer Center, Washington University School of Medicine, St. Louis, MO, 63110, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2003), 100(16), 9506-9511
CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

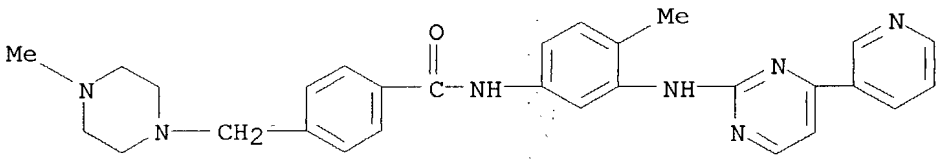
AB The t(8;21)(q22;q22) translocation, occurring in 40% of patients with acute myeloid leukemia (AML) of the FAB-M2 subtype (AML with maturation), results in expression of the RUNX1-CBF2T1 [AML1-ETO (AE)] fusion oncogene. AML/ETO may contribute to leukemogenesis by interacting with nuclear core-pressor complexes that include histone deacetylases, which mediate the repression of target genes. However, expression of AE is not sufficient to transform primary hematopoietic cells or cause disease in animals, suggesting that addnl. mutations are required. Activating mutations in receptor tyrosine kinases (RTK) are present in at least 30% of patients with AML. To test the hypothesis that activating RTK mutations cooperate with AE to cause leukemia, we transplanted retrovirally transduced murine bone marrow coexpressing TEL-PDGFRB and AE into lethally irradiated syngeneic mice. These mice (19/19, 100%) developed AML resembling M2-AML that was transplantable in secondary recipients. In contrast, control mice coexpressing with TEL-PDGFRB and a DNA-binding-mutant of AE developed a non-transplantable myeloproliferative disease identical to that induced by TEL-PDGFRB alone. We used this

unique model of AML to test the efficacy of pharmacol. inhibition of histone deacetylase activity by using trichostatin A and suberoy-lanilide hydroxamic acid alone or in combination with the tyrosine kinase inhibitor, imatinib mesylate. We found that although imatinib prolonged the survival of treated mice, histone deacetylase inhibitors provided no addnl. survival benefit. These data demonstrate that an activated RTK can cooperate with AE to cause AML in mice, and that this system can be used to evaluate novel therapeutic strategies.

IT **152459-95-5**, Imatinib
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(although imatinib prolonged the survival of treated mice, histone deacetylase inhibitors provided no addnl. survival benefit)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)

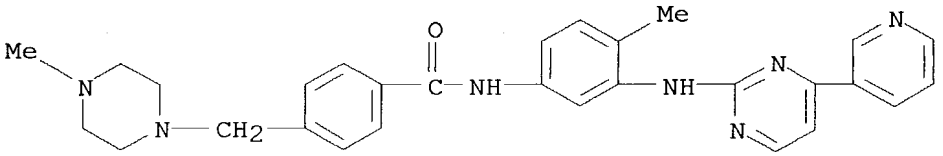


RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 15 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:551338 CAPLUS
DN 139:111702
TI Compositions and methods using ATP-dependent γ-secretase modulators for prevention and treatment of amyloid-β peptide-related disorders, and screening methods for modulators of Aβ
IN Netzer, William J.; Greengard, Paul; Xu, Huaxi
PA The Rockefeller University, USA
SO PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003057165	A2	20030717	WO 2003-US249	20030106
	WO 2003057165	A3	20031113		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
				US 2002-345009PP	20020104
	US 2004028673	A1	20040212	US 2003-337261	20030106
				US 2002-345009PP	20020104

OS MARPAT 139:111702
AB The invention provides methods and compns. for modulating levels of amyloid-β peptide (Aβ) exhibited by cells or tissues. The invention also provides pharmaceutical compns. and methods of screening for compds. that modulate Aβ levels. The invention also provides modulation of Aβ levels via selective modulation (e.g., inhibition) of ATP-dependent γ-secretase activity. The invention also provides methods of preventing, treating or ameliorating the symptoms of a disorder, including but not limited to an Aβ-related disorder, by administering a modulator of γ-secretase, including, but not limited to, a selective inhibitor of ATP-dependent γ-secretase activity or an agent that decreases the formation of active (or optimally active) γ-secretase. The invention also provides the use of inhibitors of ATP-dependent γ-secretase activity to prevent, treat or ameliorate the symptoms of Alzheimer's disease.
IT **152459-95-5D**, derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ATP-dependent enzyme modulators for prevention and treatment of amyloid-β peptide-related disorders, and screening methods for modulators of Aβ)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



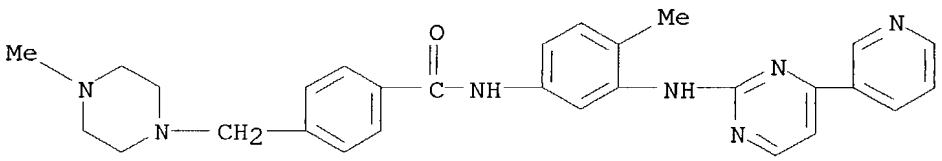
L18 ANSWER 16 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:473989 CAPLUS
DN 139:131661
TI Elevated serum tryptase levels identify a subset of patients with a myeloproliferative variant of idiopathic hypereosinophilic syndrome associated with tissue fibrosis, poor prognosis, and imatinib responsiveness
AU Klion, Amy D.; Noel, Pierre; Akin, Cem; Law, Melissa A.; Gilliland, D. Gary; Cools, Jan; Metcalfe, Dean D.; Nutman, Thomas B.
CS Laboratory of Parasitic Diseases and the Laboratory of Allergic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA
SO Blood (2003), 101(12), 4660-4666
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Since serum tryptase levels are elevated in some patients with myeloproliferative disorders, we examined their utility in identifying a subset of patients with hypereosinophilic syndrome (HES) and an underlying myeloproliferative disorder. Elevated serum tryptase levels (> 11.5 ng/mL) were present in 9 of 15 patients with HES and were associated with other markers of myeloproliferation, including elevated B12 levels and splenomegaly. Although bone marrow biopsies in these patients showed

increased nos. of CD25+ mast cells and atypical spindle-shaped mast cells, patients with HES and elevated serum tryptase could be distinguished from patients with systemic mastocytosis and eosinophilia by their clin. manifestations, the absence of mast cell aggregates, the lack of a somatic KIT mutation, and the presence of the recently described fusion of the Fip1-like 1 (FIP1L1) gene to the **platelet**-derived growth factor receptor α gene (PDGFRA). Patients with HES and elevated serum tryptase were more likely to develop fibro-proliferative end organ damage, and 3 of 9 died within 5 yr of diagnosis in contrast to 0 of 6 patients with normal serum tryptase levels. All 6 patients with HES and elevated tryptase treated with imatinib demonstrated a clin. and hematol. response. In summary, elevated serum tryptase appears to be a sensitive marker of a myeloproliferative variant of HES that is characterized by tissue fibrosis, poor prognosis, and imatinib responsiveness.

IT **152459-95-5**, Imatinib
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(elevated serum tryptase appears as marker of myeloproliferative variant of idiopathic hypereosinophilic syndrome associated with tissue fibrosis, poor prognosis and imatinib responsiveness)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

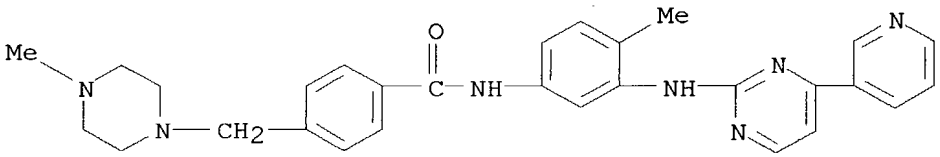
L18 ANSWER 17 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:447424 CAPLUS
DN 139:127599
TI Sensitivity to imatinib but low frequency of the TEL/PDGFRβ fusion protein in chronic myelomonocytic leukemia
AU Gunby, Rosalind Helen; Cazzaniga, Giovanni; Tassi, Elena; le Coutre, Philipp; Pogliani, Enrico; Specchia, Giorgina; Biondi, Andrea; Gambacorti-Passerini, Carlo
CS Department of Experimental Oncology, Istituto Nazionale Tumori, Milan, 20133, Italy
SO Haematologica (2003), 88(4), 408-415
CODEN: HAEMAX; ISSN: 0390-6078
PB Ferrata Storti Foundation
DT Journal
LA English
AB Chronic myelomonocytic leukemia (CMML) is a myelodysplastic syndrome that was associated with the expression of **platelet**-derived growth factor β receptor (PDGFRβ) fusion proteins, namely TEL/PDGFRβ. These fusion proteins possess a constitutive PDGFRβ tyrosine kinase activity, leading to aberrant PDGFRβ signaling and cellular transformation. The expression of PDGFRβ fusions in CMML could have therapeutic relevance, as PDGFRβ is inhibited by the selective tyrosine kinase inhibitor, imatinib. Here, the authors investigated the possibility of employing imatinib to treat CMML. We

assessed the effect of imatinib on TEL/PDGFRβ transformed cells in terms of proliferation, by trypan blue exclusion and 3H-thymidine uptake, and TEL/PDGFRβ autophosphorylation by anti-phosphotyrosine immunoblotting. TEL/PDGFRβ expression in mononuclear cells from the peripheral blood of 27 clin. diagnosed CMML patients was determined by reverse transcriptase-polymerase chain reaction. Imatinib potently inhibited the proliferation of TEL/PDGFRβ transformed cells (IC50=7.5 nM), and TEL/PDGFRβ kinase activity. However, TEL/PDGFRβ expression was detected in only 1 of 27 CMML patients (4%, confidence intervals: 0-13%). Addnl., another PDGFRβ fusion protein, Hip1/PDGFRβ, had a similarly low incidence in the same samples: 1 of 25 (4%, confidence intervals: 0-14%). Although imatinib represents an attractive therapeutic agent for neoplasias associated with abnormal PDGFRβ signaling, the low frequency of the TEL/PDGFRβ and Hip1/PDGFRβ fusion proteins in CMML suggests that its application to this disease maybe limited. Detection of PDGFRβ fusion genes in individual patients is necessary to employ this drug rationally in CMML.

IT **152459-95-5**, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imatinib inhibited proliferation and kinase activity of TEL/PDGFRβ transformed cells in chronic myelomonocytic leukemia)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:417591 CAPLUS
DN 138:406583
TI An inhibitor of receptor tyrosine kinases for treating hair depigmentation
IN Mahon, Francois-Xavier; Cony-Makhoul, Pascale; Etienne, Gabriel
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003043591	A1	20030530	WO 2002-EP13021	20021120

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT,

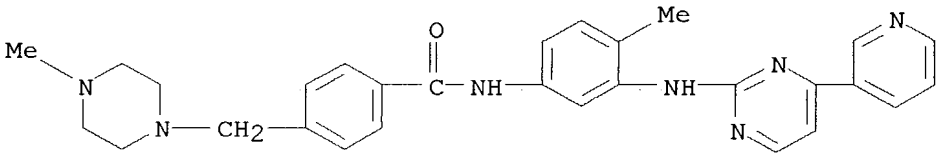
LU, MC, NL, PT, SE, SK, TR
GB 2001-27922 A 20011121

AB The invention relates to a method of treating a warm-blooded animal, especially a human, having depigmented hair or subject to hair depigmentation comprising at least one inhibitor of Abelson tyrosine kinase (Abl), receptor tyrosine kinase and/or **platelet**-derived growth factor (PDGF) receptor tyrosine kinase, and a cosmetically acceptable carrier, to retard, prevent, suppress, and/or reverse the depigmentation of hair. The use of the above compound for the preparation of a pharmaceutical for the treatment of a disease characterized by hair depigmentation is described. In a clin. study 9 patients with a confirmed diagnosis of Philadelphia chromosome-pos. CML (chronic myelogenous leukemia) received treatment with orally administered imatinib (400 or 600 mg). These patients have presented progressive hair repigmentation under the above drug treatment.

IT **152459-95-5**, Imatinib
RL: COS (Cosmetic use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor of receptor tyrosine kinases for treating hair depigmentation)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 19 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:413877 CAPLUS
DN 138:396218
TI Combination for the treatment of endothelial damage
IN Alitalo, Kari; Heldin, Carl Henrik; Leppanen, Olli; Ostman, Arne; Yla-Herttuala, Seppo
PA Finland
SO U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003099687	A1	20030529	US 2002-227081	20020823
			GB 2001-20690 A	20010824

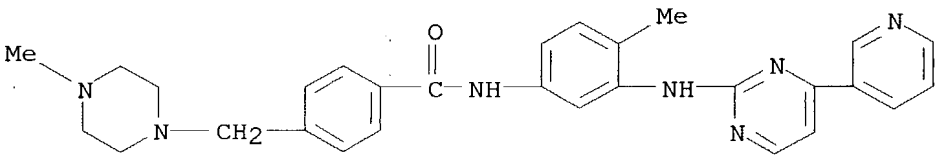
AB The invention relates to a combination of (a) an inhibitor of **platelet**-derived growth factor (PDGF) activity and (b) a vector for vascular endothelial growth factor (VEGF-, especially VEGF-C) gene transfer,
a pharmaceutical preparation comprising (a) and (b) in combination together with a pharmaceutically acceptable carrier material; a product comprising (a) and (b) as defined above and optionally a pharmaceutically acceptable carrier material, for simultaneous, chronol. staggered or sep. use; a

method of administering or the use of said combination or product for the treatment of endothelial damage; and/or to the use of (a) and (b) for the manufacture of said pharmaceutical preparation or product for the treatment of endothelial damage.

IT **152459-95-5**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination for treatment of vascular endothelial damage using **platelet**-derived growth factor inhibitors and gene transfer of vascular endothelial growth factor in relation to formulation and pharmacokinetics)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



L18 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:322631 CAPLUS

DN 139:349260

TI Chronic allograft nephropathy is prevented by inhibition of **platelet**-derived growth factor receptor: tyrosine kinase inhibitors as a potential therapy

AU Savikko, Johanna; Taskinen, Eero; von Willebrand, Eva

CS Transplantation Laboratory, Haartman Institute, University of Helsinki and Helsinki University Central Hospital, University of Helsinki, Finland

SO Transplantation (2003), 75(8), 1147-1153
CODEN: TRPLAU; ISSN: 0041-1337

PB Lippincott Williams & Wilkins

DT Journal

LA English

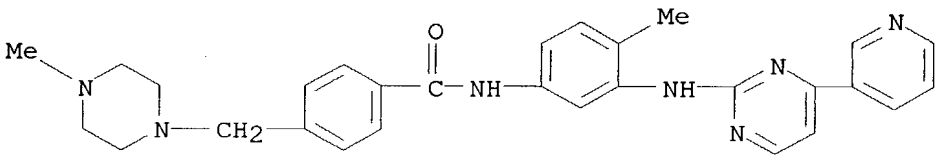
AB Chronic allograft nephropathy (CAN) is the primary reason for late allograft loss in kidney transplantation, and currently there is no treatment available for it. **Platelet**-derived growth factor (PDGF) is suggested to be a major mitogen mediating mesenchymal cell proliferation in CAN. It has been shown that PDGF is already induced at acute renal allograft rejection, indicating a link between acute rejection and subsequent development of CAN. However, the definite effect of PDGF on the pathogenesis of CAN is still unknown. We investigated the role of PDGF in CAN by inhibiting PDGF by imatinib (STI571), a selective PDGF receptor tyrosine kinase inhibitor. Kidney transplantations were performed from Dark Agouti (DA) to Wistar-Furth rats, and syngenic control transplantations were performed from DA to DA rats. All allograft recipients were immunosuppressed with cyclosporine A (1.5 mg/kg/day s.c.). One group of the animals was also treated with imatinib (10 mg/kg/day orally). Serum creatinine levels and cyclosporine A concns. were measured once per wk until the animals were killed. Grafts were harvested 5 and 90 days after transplantation for histol. and immunohistochem. Only very few histol. chronic changes, similar to syngenic grafts, were seen in imatinib-treated allografts compared with control allografts. Creatinine values of imatinib-treated allograft recipients and infiltration of

inflammatory cells, PDGF ligand, and receptor induction were also at the same level as in syngenic grafts. Our results demonstrate that imatinib prevents CAN almost completely, indicating that PDGF plays an important role in its pathogenesis. On the basis of our findings, imatinib could be a potential intervention in preventing CAN in clin. kidney transplantation.

IT **152459-95-5**, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PDGFR role in chronic allograft nephropathy pathogenesis and PDGFR tyrosine kinase inhibitors as potential therapy)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 21 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:244948 CAPLUS

DN 139:301661

TI A tyrosine kinase created by fusion of the PDGFRA and FIP1L1 genes as a therapeutic target of imatinib in idiopathic hypereosinophilic syndrome

AU Cools, Jan; Daniel, Ph. D.; DeAngelo, J.; Gotlib, Jason; Stover, Elizabeth H.; Phil, M.; Legare, robert D.; Cortes, Jorges; Lutok, Jeffrey; Clark, Jennifer; Galinsky, Ilene; Griffin, James D.; Cross, Nicholas, C. P.; Tefferi, Ayalew; Malone, James; Alam, Fafeul; Schrier, Stanley L.; Schmid, Janet; Rose, Michal; Vandenberghe, Peter; Verhoef, Gregor; Boogaerts, Marc; Wlodarska, Iwona; Kantarjian, Hagop; Marynen, Peter; Coutre, Steven E.; Stone, Richard; Gilliland, D. Gary

CS Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

SO New England Journal of Medicine (2003), 348(13), 1201-1214
CODEN: NEJMAG; ISSN: 0028-4793

PB Massachusetts Medical Society

DT Journal

LA English

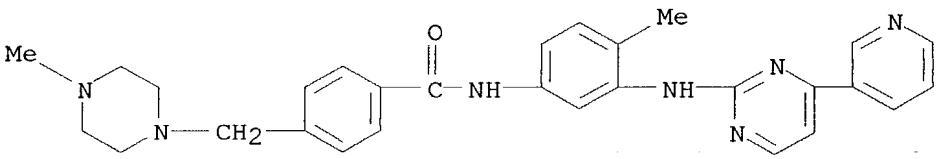
AB Idiopathic hypereosinophilic syndrome involves a prolonged state of eosinophilia associated with organ dysfunction. It is of unknown cause. Recent reports of responses to imatinib in patients with the syndrome suggested that an activated kinase such as ABL, **platelet**-derived growth factor receptor (PDGFR), or KIT, all of which are inhibited by imatinib, might be the cause. We treated 11 patients with the hypereosinophilic syndrome with imatinib and identified the mol. basis for the response. Nine of the 11 patients treated with imatinib had responses lasting more than three months in which the eosinophil count returned to normal. One such patient had a complex chromosomal abnormality, leading to the identification of a fusion of the Fip1H-like 1 (FIP1L1) gene to the PDGFRα (PDGFRA) gene generated by an interstitial deletion on chromosome 4q12. FIP1L1-PDGFRα is a constitutively activated tyrosine kinase that transforms hematopoietic cells and is inhibited by

imatinib (50 % inhibitory concentration, 3.2 nM). The FIP1L1-PDGFRA fusion gene was subsequently detected in 9 of 16 patients with the syndrome and in 5 of the 9 patients with responses to imatinib that lasted more than three months. Relapse in one patient correlated with the appearance of a T674I mutation in PDGFRA that confers resistance to imatinib. The hypereosinophilic syndrome may result from a novel fusion tyrosine kinase-FIP1L1-PDGFRα-that is a consequence of an interstitial chromosomal deletion. The acquisition of a T674I resistance mutation at the time of relapse demonstrates that FIP1L1-PDGFRα is the target of imatinib. Our data indicate that the deletion of genetic material may result in gain-of-function fusion proteins.

IT **152459-95-5,** Imatinib
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of imatinib on tyrosine kinase created by fusion of PDGFRA and FIP1L1 genes in idiopathic hypereosinophilic syndrome)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

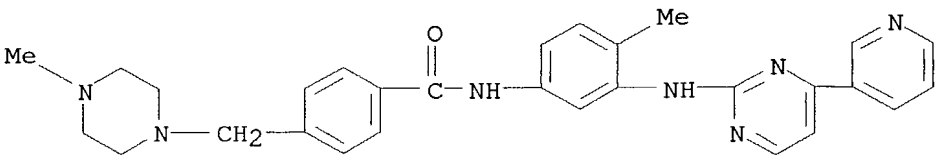
L18 ANSWER 22 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:223318 CAPLUS
DN 138:378776
TI High levels of BAX, low levels of MRP-1, and high platelets are independent predictors of response to imatinib in myeloid blast crisis of CML
AU Lange, Thoralf; Gunther, Christine; Kohler, Thomas; Krahl, Rainer; Musiol, Scarlet; Leiblein, Sabine; Al-Ali, Haifa-Kathrin; van Hoomissen, Iris; Niederwieser, Dietger; Deininger, Michael W. N.
CS Department of Hematology, University of Leipzig, Germany
SO Blood (2003), 101(6), 2152-2155
CODEN: BLOOAW; ISSN: 0006-4971
PB American Society of Hematology
DT Journal
LA English
AB Imatinib induces remissions in approx. 30% of patients with chronic myeloid leukemia (CML) in myeloid blast crisis (M-BC). Because most patients eventually relapse, allogeneic stem cell transplantation (SCT) in remission offers the best chance for cure. Remission induction with imatinib alone would seem ideal because it is less toxic than conventional chemotherapy. Conversely, patients unlikely to respond may benefit from combination therapy up front. To identify prognostic factors, we studied the mRNA expression of genes related to drug resistance and apoptosis in leukemic cells from patients with M-BC and their in vitro sensitivity to imatinib, and analyzed the results with other baseline factors for their impact on response. We show that high levels of BAX, low levels of MRP-1,

and a high **platelet** count are independently predictive of response to imatinib. Combined into a score, these parameters may be clin. useful for risk-adapted patient stratification.

IT **152459-95-5**, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BAX, MRP-1, and platelets as independent predictors of response to imatinib in myeloid blast crisis of CML)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 23 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:154278 CAPLUS

DN 138:198670

TI GnRh agonist combination drugs

IN Furuya, Shuichi; Kusaka, Masami

PA Takeda Chemical Industries, Ltd., Japan

SO PCT Int. Appl., 73 pp.
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003015820	A1	20030227	WO 2002-JP8130	20020808

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

			JP 2001-244616 A	20010810
JP 2003137814	A2	20030514	JP 2002-231922	20020808
			JP 2001-244616 A	20010810

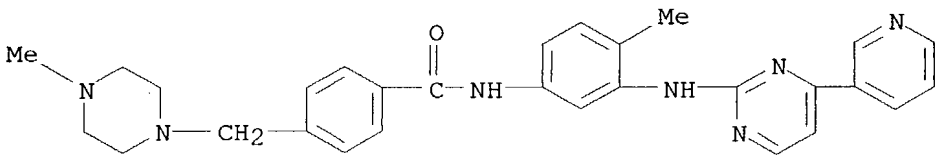
AB In the field of pharmaceuticals, it is intended to provide drugs whereby the preventive and therapeutic effects of a GnRH agonist on various diseases can be enhanced and QOL can be improved. More specifically, combination drugs characterized in that the GnRH agonist is combined with a chemical selected from among SERM, SARM, sex hormone synthesis inhibitors, receptor-type tyrosine kinase inhibitors, bone metabolism regulators, drugs for immunotherapy, cytokine/chemokine inhibitors and endothelin receptor antagonists. Owing to these combinations, excellent effects of enhancing

the preventive and therapeutic effects of the GnRH agonist on various diseases and relieving side effects can be established. Furthermore, QOL can be improved thereby.

IT **152459-95-5**, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GnRH agonist combination drugs for treating various diseases and relieving side effects)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 24 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:61253 CAPLUS

DN 139:30316

TI Juxtamembrane mutant V560GKit is more sensitive to Imatinib (STI571) compared with wild-type c-Kit whereas the kinase domain mutant D816VKit is resistant

AU Frost, Michelle J.; Ferrao, Petranel T.; Hughes, Timothy P.; Ashman, Leonie K.

CS Discipline of Medical Biochemistry, School of Biomedical Sciences, University of Newcastle, Callaghan, 2308, Australia

SO Molecular Cancer Therapeutics (2002), 1(12), 1115-1124
CODEN: MCTOCF; ISSN: 1535-7163

PB American Association for Cancer Research

DT Journal

LA English

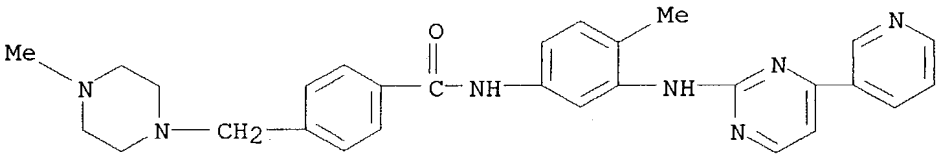
AB Imatinib (Glivec; STI571) is an ATP-competitive kinase inhibitor of c-Abl, BCR/ABL, c-Kit, and **platelet**-derived growth factor receptor. Overexpression or constitutive activation of Kit by mutations have been associated with various malignancies. Mutations in the intracellular juxtamembrane region of Kit (e.g., V560G) are common in gastrointestinal stromal tumors and have been linked to poor prognosis. Mutations in the kinase domain of Kit (e.g., D816V) have been detected in mastocytosis, acute myeloid leukemia, and germ-cell tumors. To determine the sensitivity of Kit mutants to Imatinib in the same cellular background, wild-type Kit (WTKit), V560GKit and D816VKit were expressed in FDC-P1 cells. Growth of FDC(WTKit) was inhibited by Imatinib with GI50 (a concentration of drug at which 50% inhibition of growth occurs) of 0.1-0.2 μM but FDC(V560GKit) were more sensitive to Imatinib with a GI50 of 0.01-0.025 μM and FDC(D816VKit) were resistant to Imatinib with a GI50 greater than 5 μM. The naturally occurring isoforms of c-Kit did not differ in their sensitivity to Imatinib. Immunopptn. and Western blot anal. indicated that 1 μM Imatinib reduced phosphorylation of WTKit and completely blocked phosphorylation of V560GKit but did not affect D816VKit phosphorylation. In signaling studies, addition of stem cell factor (SCF)

induced phosphorylation of ERK and Akt by WTKit, and ERK, Akt and STAT3 by V560GKit, which were all blocked by Imatinib. Imatinib also blocked the constitutive activation of Akt and STAT3 by V560GKit but had no affect on the constitutive activation of ERK, Akt, and STAT3 by D816VKit. Overall, these findings demonstrate the increased susceptibility of the Kit juxtamembrane mutant, V560G, and the resistance of the kinase domain mutant, D816V, to Imatinib compared with WTKit.

IT **152459-95-5**, Imatinib
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(juxtamembrane mutant V560GKit is more sensitive to Imatinib compared with wild-type c-Kit whereas the kinase domain mutant D816VKit is resistant)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:22677 CAPLUS
DN 138:95589
TI Use of tyrosine kinase inhibitors for treating autoimmune diseases
IN Moussy, Alain; Kinet, Jean-Pierre
PA AB Science, Fr.
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 13

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003002109	A2	20030109	WO 2002-IB3302	20020628
WO 2003002109	C1	20030501		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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	US 2001-301405PP 20010629
	US 2001-301409PP 20010629
	US 2001-301410PP 20010629
	US 2001-341273PP 20011220

PATENT FAMILY INFORMATION:

FAN 2003:22673

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003002105	A2	20030109	WO 2002-IB3288	20020628
	WO 2003002105	A3	20030828		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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US 2001-301411PP 20010629

	EP 1401411	A2	20040331	EP 2002-755506	20020628

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2001-301411PP 20010629

WO 2002-IB3288 W 20020628

FAN 2003:22674

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003002106	A2	20030109	WO 2002-IB3297	20020628
	WO 2003002106	A3	20030530		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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US 2001-301408PP 20010629

	EP 1401413	A2	20040331	EP 2002-755512	20020628

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2001-301408PP 20010629

WO 2002-IB3297 W 20020628

FAN 2003:22675

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003002107	A2	20030109	WO 2002-IB3298	20020628
	WO 2003002107	A3	20031002		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-301409PP 20010629

	EP 1401414	A2	20040331	EP 2002-758692	20020628

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2001-301409PP 20010629
WO 2002-IB3298 W 20020628

FAN 2003:22676

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003002108	A2	20030109	WO 2002-IB3301	20020628
	WO 2003002108	A3	20030925		

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US 2001-301410PP 20010629

	EP 1401415	A2	20040331	EP 2002-758693	20020628

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2001-301410PP 20010629
WO 2002-IB3301 W 20020628

FAN 2003:22681

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003002114	A2	20030109	WO 2002-IB3303	20020628
	WO 2003002114	A3	20030925		

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US 2001-301406PP 20010629

	EP 1401429	A2	20040331	EP 2002-755513	20020628

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US 2001-301406PP 20010629
WO 2002-IB3303 W 20020628

FAN 2003:23102

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003003004	A2	20030109	WO 2002-IB3294	20020628

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2001-301404PP 20010629
US 2001-301405PP 20010629
US 2001-301406PP 20010629
US 2001-301407PP 20010629
US 2001-301408PP 20010629
US 2001-301409PP 20010629
US 2001-301410PP 20010629
US 2001-301411PP 20010629
US 2001-323313PP 20010920
US 2001-323314PP 20010920
US 2001-323315PP 20010920
US 2001-22842 A 20011220
US 2003091974 A1 20030515 US 2001-22842 20011220
US 2001-301404PP 20010629
US 2001-301405PP 20010629
US 2001-301406PP 20010629
US 2001-301407PP 20010629
US 2001-301408PP 20010629
US 2001-301409PP 20010629
US 2001-301410PP 20010629
US 2001-301411PP 20010629
US 2001-323313PP 20010920
US 2001-323314PP 20010920
US 2001-323315PP 20010920

FAN 2003:23103

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003003006	A2	20030109	WO 2002-IB3296	20020628

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-301404PP 20010629

FAN 2003:42089

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003004006	A2	20030116	WO 2002-IB3295	20020628
	WO 2003004006	A3	20030530		
	WO 2003004006	C1	20030821		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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US 2001-301407PP 20010629

EP 1401412 A2 20040331 EP 2002-755510 20020628

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2001-301407PP 20010629
WO 2002-IB3295 W 20020628

FAN 2003:42090

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003004007	A2	20030116	WO 2002-IB3317	20020628
	WO 2003004007	A3	20030828		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-301405PP 20010629

	EP 1401416	A2	20040331	EP 2002-758697	20020628

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2001-301405PP 20010629
WO 2002-IB3317 W 20020628

FAN 2003:242116

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003024386	A2	20030327	WO 2002-IB4236	20020920
	WO 2003024386	A3	20040205		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-323315PP 20010920

FAN 2003:334887

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003035049	A2	20030501	WO 2002-IB4251	20020920

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-323313PP 20010920

FAN 2003:334888

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 2003035050	A2	20030501	WO 2002-IB4290	20020920

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-323314PP 20010920

OS MARPAT 138:95589

AB The present invention relates to a method for treating autoimmune diseases, more particularly selected from the group consisting of multiple sclerosis, ulcerative colitis, Crohn's disease, rheumatoid arthritis and polyarthritis, scleroderma, lupus erythematosus, dermatomyositis, pemphigus, polymyositis, vasculitis, as well as graft- vs. host diseases, comprising administering a compound capable of depleting mast cells to a mammal in need of such treatment. Such compds. can be chosen from tyrosine kinase inhibitors and more particularly non-toxic, selective and potent c-kit inhibitors. Preferably, said inhibitor is unable to promote death of IL-3 dependent cells cultured in presence of IL-3.

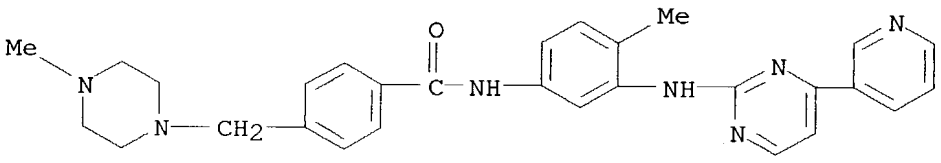
IT **152459-95-5**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of tyrosine kinase inhibitors for treating autoimmune diseases)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



L18 ANSWER 26 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:778718 CAPLUS

DN 137:289046

TI Methods and compositions for enhancing pharmaceutical treatments

IN Newman, Michael J.; Dixon, William Ross

PA USA

SO U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S. Ser. No. 684,293.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002147197	A1	20021010	US 2002-104549	20020320
				US 1999-158322PP	19991008
				US 2000-684293 A2	20001006

PATENT FAMILY INFORMATION:

FAN 2001:283724

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001026467	A1	20010419	WO 2000-US27612	20001006
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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				US 1999-158322PP	19991008
	EP 1221847	A1	20020717	EP 2000-968797	20001006
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
				US 1999-158322PP	19991008
				WO 2000-US27612W	20001006
	JP 2003511396	T2	20030325	JP 2001-529267	20001006
				US 1999-158322PP	19991008
				WO 2000-US27612W	20001006

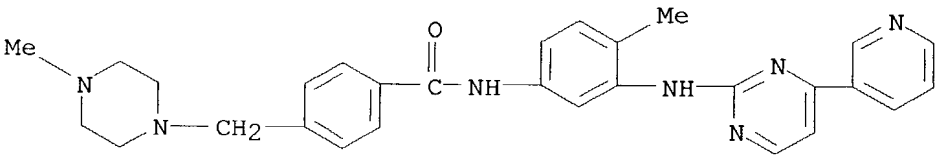
OS MARPAT 137:289046

AB Improved methods are provided for therapeutic and/or preventative treatment to a mammal in which the mammal is protected against the toxicity of active pharmaceutical agents that (i) bind to or are substrates for P-gp, (ii) are taxane analogs, and/or (iii) are inhibitors of tubulin disassembly. Addnl. provided are compns. and methods useful for treating cell proliferative disorders. Further provided are methods of increasing the bioavailability of therapeutic and/or preventative treatments in a mammal. Particular embodiments are directed to increasing such bioavailability across the blood-brain barrier.

IT **152459-95-5**, Imatinib **152459-95-5D**, Imatinib, derivs., analogs, and metabolites
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for enhancing pharmaceutical treatments)

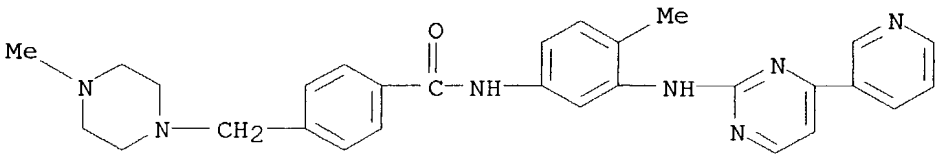
RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



L18 ANSWER 27 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:489219 CAPLUS
DN 135:71265
TI Combinations of a receptor tyrosine kinase inhibitor with an organic compound capable of binding to α1-acidic glycoprotein
IN Gambacorti-Passerini, Carlo; Lecoutre, Philipp
PA Novartis A.-G., Switz.; Novartis-Erfindungen
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001047507	A2	20010705	WO 2000-EP13161	20001222
	WO 2001047507	A3	20020404		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
				IT 1999-MI2711 A	19991227
	BR 2000016817	A	20021001	BR 2000-16817	20001222
				IT 1999-MI2711 A	19991227
				WO 2000-EP13161W	20001222
	EP 1250140	A2	20021023	EP 2000-985244	20001222
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				IT 1999-MI2711 A	19991227
				WO 2000-EP13161W	20001222
	JP 2003523325	T2	20030805	JP 2001-548102	20001222
				IT 1999-MI2711 A	19991227
				WO 2000-EP13161W	20001222
	US 2003125343	A1	20030703	US 2002-169035	20021007
				IT 1999-MI2711 A	19991227
				WO 2000-EP31361W	20001222

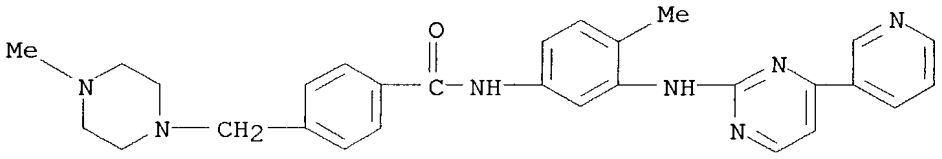
OS MARPAT 135:71265
AB This invention relates to combinations of an abl-, PDGF-Receptor-and/or Kit receptor-tyrosine kinase inhibitor with an organic compound capable of binding to α1-acidic glycoprotein (AGP), as well as to pharmaceutical prepns. and/or therapies, in relation to disease states which respond to inhibition of abl-, PDGF-Receptor- and/or Kit-receptor tyrosine kinase. In particular, the invention relates to products or combinations comprising and abl-, PDGF-Receptor- and/or Kit receptor-tyrosine kinase inhibitor with an organic compound capable of binding to AGP, either in fixed combination or for chronol. staggered or

simultaneous administration, and the combined used of both classes of compds., either in fixed combination or for chronol. staggered or simultaneous administration, for the treatment of proliferative diseases, especially tumor diseases, especially those that can be treated by inhibition of abl-,
PDGF-Receptor- and/or Kit receptor-tyrosine kinase activity.

IT **152459-95-5**, cgp57148
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antitumor combinations of a receptor tyrosine kinase inhibitor with an organic compound capable of binding to α1-acidic glycoprotein)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



L18 ANSWER 28 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:307258 CAPLUS

DN 134:361796

TI PDGF signal transduction inhibition ameliorates experimental mesangial proliferative glomerulonephritis

AU Gilbert, Richard E.; Kelly, Darren J.; McKay, Tara; Chadban, Steven; Hill, Prudence A.; Cooper, Mark E.; Atkins, Robert C.; Nikolic-Paterson, David J.

CS Department of Medicine, St. Vincent's Hospital, University of Melbourne, Austin, Australia

SO Kidney International (2001), 59(4), 1324-1332
CODEN: KDYIA5; ISSN: 0085-2538

PB Blackwell Science, Inc.

DT Journal

LA English

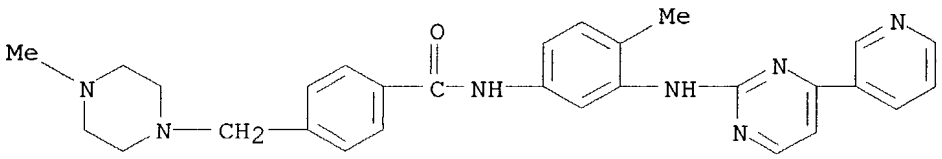
AB **Platelet**-derived growth factor (PDGF) has been consistently implicated in the cell proliferation and extracellular matrix accumulation, which characterize progressive glomerular disease. In the present study, the effects of a potent and selective inhibitor of PDGF receptor tyrosine kinase, STI 571, were examined in vitro and in vivo. Cultured mesangial cells were incubated with PDGF (50 ng/mL) and fibroblast growth factor-2 (FGF-2; 50 ng/mL) and treated with STI 571 (0.13 to 2.0 μM). Exptl. mesangial proliferative glomerulonephritis was induced in male Wistar rats with monoclonal OX-7, anti-rat Thy-1.1 antibody with rats randomized to receive either STI 571 (50 mg/kg i.p. daily) or vehicle. Animals were examined six days later. In vitro, both PDGF and FGF-2 induced a threefold increase in mesangial cell 3H-thymidine incorporation. STI 571 reduced PDGF but not FGF-2-stimulated mesangial cell proliferation in a dose-dependent manner, with complete abolition at 0.4 μM. In animals with Thy-1.1 glomerulonephritis, PDGF receptor tyrosine kinase blockade was associated with significant redns. in mesangial cell proliferation, the number of activated (α-smooth muscle pos.) mesangial cells, and glomerular type IV collagen deposition. Amelioration

of the pathol. of exptl. mesangial proliferative glomerulonephritis by blockade of PDGF receptor activity suggests the potential clin. utility of this approach as a therapeutic strategy in glomerular disease.

IT **152459-95-5**, STI 571
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PDGF signal transduction inhibition amelioration of exptl. mesangial proliferative glomerulonephritis and mechanisms thereof)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 29 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:493544 CAPLUS
DN 133:129892
TI High affinity enzyme inhibitors and therapeutic uses thereof
IN Shokat, Kevan M.
PA Princeton University, USA
SO PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000042042	A2	20000720	WO 2000-US551	20000111
WO 2000042042	A3	20001102		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
			US 1999-115340PP	19990111
			US 1999-145422PP	19990723
EP 1140938	A2	20011010	EP 2000-904268	20000111
EP 1140938	B1	20030827		
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			US 1999-115340PP	19990111
			US 1999-145422PP	19990723
			WO 2000-US551 W	20000111
US 6383790	B1	20020507	US 2000-480993	20000111

				US 1999-115340PP	19990111
				US 1999-145422PP	19990723
	JP 2002534524	T2	20021015	JP 2000-593609	20000111
				US 1999-115340PP	19990111
				US 1999-145422PP	19990723
				WO 2000-US551 W	20000111
	EP 1321467	A2	20030625	EP 2003-5036	20000111
	EP 1321467	A3	20031008		
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				US 1999-145422PP	19990723
				EP 2000-904268 A3	20000111
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				US 1999-115340PP	19990111
				US 1999-145422PP	19990723
				WO 2000-US551 W	20000111
	US 2003073218	A1	20030417	US 2002-44967	20020529
				US 1999-115340PP	19990111
				US 1999-145422PP	19990723
				US 2000-480993 A1	20000111

PATENT FAMILY INFORMATION:

FAN 2001:78571

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001007659	A2	20010201	WO 2000-US19912	20000721
	WO 2001007659	A3	20010322		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
				US 1999-145422PP	19990723
				US 2000-621293 A	20000720
	EP 1321467	A2	20030625	EP 2003-5036	20000111
	EP 1321467	A3	20031008		
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				US 1999-115340PP	19990111
				US 1999-145422PP	19990723
				EP 2000-904268 A3	20000111
	US 6610483	B1	20030826	US 2000-621293	20000720
				US 1999-145422PP	19990723
	EP 1196626	A2	20020417	EP 2000-950527	20000721
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				US 2000-621293 A	20000720
				WO 2000-US19912W	20000721
	JP 2003521890	T2	20030722	JP 2001-512924	20000721
				US 1999-145422PP	19990723
				US 2000-621293 A	20000720
				WO 2000-US19912W	20000721
	US 2003073218	A1	20030417	US 2002-44967	20020529
				US 1999-115340PP	19990111

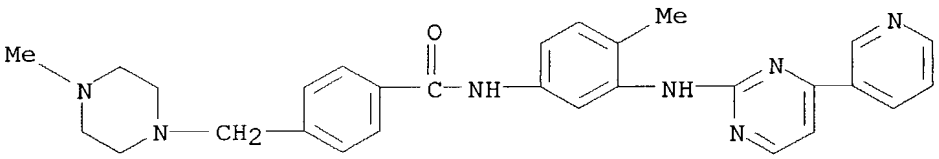
US 1999-145422PP 19990723
US 2000-480993 A120000111

AB The invention provides general methods for discovering mutant inhibitors for any class of enzymes as well as the specific inhibitors so identified. More specifically, the invention provides general methods for discovering specific inhibitors for multi-substrate enzymes. Examples of such multi-substrate enzymes include, but are not limited to, kinases and transferases. The mutant inhibitors identified by the methods of the invention can be used to highly selectively disrupt cell functions such as oncogenic transformation. In one particular example, the invention provides an Src protein kinase inhibitor, pharmaceutical compns. thereof and methods of disrupting transformation in a cell that expresses the target v-src comprising contacting the cell with the protein kinase inhibitor.

IT **152459-95-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(high affinity enzyme inhibitors and therapeutic uses)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



L18 ANSWER 30 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:413549 CAPLUS

DN 131:223278

TI Selective tyrosine kinase inhibitor for the **platelet**-derived growth factor receptor in vitro inhibits smooth muscle cell proliferation after reinjury of arterial intima in vivo

AU Myllarniemi, Marjukka; Frosen, Juhana; Ramirez, Lazaro G. Calderon; Buchdunger, Elisabeth; Lemstrom, Karl; Hayry, Pekka

CS Transplantation Laboratory, University of Helsinki, Helsinki, FIN-00014, Finland

SO Cardiovascular Drugs and Therapy (1999), 13(2), 159-168
CODEN: CDTHET; ISSN: 0920-3206

PB Kluwer Academic Publishers

DT Journal

LA English

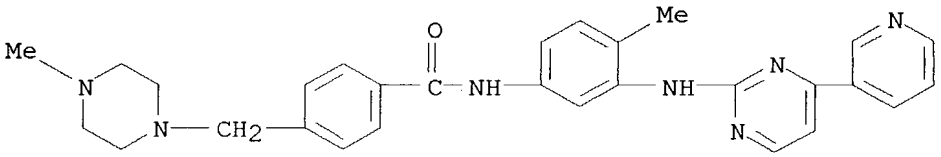
AB The long-term success of coronary angioplasty is limited by restenosis. This study was undertaken to investigate whether and to what extent the enhanced proliferative response observed in a balloon reinjury model of rat aorta is regulated by the PDGF receptor (PDGF-R). Balloon injury was performed to 14-day-old pre-existing neointimal lesion in rat aorta. PDGF receptor and ligand immunoreactivity were measured at several time points after the first and second injury, and PDGF-R signaling was blocked with a selective inhibitor of PDGF-R tyrosine kinase. In the neointima, after repeated injury, upregulation of PDGF-AA was seen to coincide with a prompt proliferative response of smooth muscle cells (SMC). Administration of the PDGF-R tyrosine kinase inhibitor in vivo, tested and found to inhibit the proliferation of SMC induced by PDGF-AA and PDGF-BB,

but not by IGF-1, EGF, or bFGF, resulted in a 60% reduction in the absolute number
and percentage of BrdU + cells after the second balloon injury to pre-existing neointima, but had no significant effect on proliferation after the first injury. Endpoint lesion area was reduced by 50% in the treated group at 14 days after the second injury. The results suggest that systemic administration of a tyrosine kinase inhibitor specific for the PDGF-R can be useful in the prevention of restenosis.

IT **152459-95-5**, CGP 57148B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(tyrosine kinase inhibitor for PDGF receptor inhibits smooth muscle cell proliferation after reinjury of arterial intima)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 31 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:153904 CAPLUS

DN 130:323679

TI TEL/PDGFβR induces hematologic malignancies in mice that respond to a specific tyrosine kinase inhibitor

AU Tomasson, Michael H.; Williams, Ifor R.; Hasserjian, Robert; Udomsakdi, Chirayu; McGrath, Shannon M.; Schwaller, Juerg; Druker, Brian; Gilliland, D. Gary

CS Division of Hematology, Brigham and Women's Hospital, Boston, MA, 02115, USA

SO Blood (1999), 93(5), 1707-1714
CODEN: BLOOAW; ISSN: 0006-4971

PB W. B. Saunders Co.

DT Journal

LA English

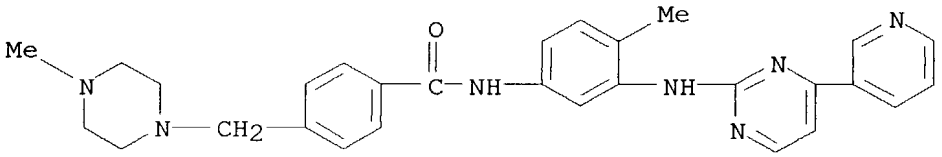
AB The TEL/PDGFβR fusion protein is expressed as the consequence of a recurring t(5;12) translocation associated with chronic myelomonocytic leukemia (CMML). Unlike other activated protein tyrosine kinases associated with hematopoietic malignancies, TEL/PDGFβR is invariably associated with a myeloid leukemia phenotype in humans. To test the transforming properties of TEL/PDGFβR in vivo, and to analyze the basis for myeloid lineage specificity in humans, the authors constructed transgenic mice with TEL/PDGFβR expression driven by a lymphoid-specific Ig enhancer-promoter cassette. These mice developed lymphoblastic lymphomas of both T and B lineage, demonstrating that TEL/PDGFβR is a transforming protein in vivo, and that the transforming ability of this fusion is not inherently restricted to the myeloid lineage. Treatment of TEL/PDGFβR transgenic animals with a protein tyrosine kinase inhibitor with in vitro activity against PDGFβR (CGP57148) resulted in suppression of disease and a prolongation of survival. A therapeutic

benefit was apparent both in animals treated before the development of overt clonal disease and in animals transplanted with clonal tumor cells. These results suggest that small-mol. tyrosine kinase inhibitors may be effective treatment for activated tyrosine kinase-mediated malignancies both early in the course of disease and after the development of addnl. transforming mutations.

IT **152459-95-5**, CGP57148
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TEL/PDGFβR fusion protein induces hematol. malignancies in mice that respond to specific tyrosine kinase inhibitor)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 32 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:791751 CAPLUS

DN 128:110519

TI CGP 57148, a tyrosine kinase inhibitor, inhibits the growth of cells expressing BCR-ABL, TEL-ABL, and TEL-PDGFR fusion proteins

AU Carroll, Martin; Ohno-Jones, Sayuri; Tamura, Shu; Buchdunger, Elisabeth; Zimmermann, Jurg; Lydon, Nicholas B.; Gilliland, D. Gary; Druker, Brian J.

CS Division of Hematology and Medical Oncology, Oregon Health Sciences University, Portland, OR, 97201-3098, USA

SO Blood (1997), 90(12), 4947-4952
CODEN: BLOOAW; ISSN: 0006-4971

PB W. B. Saunders Co.

DT Journal

LA English

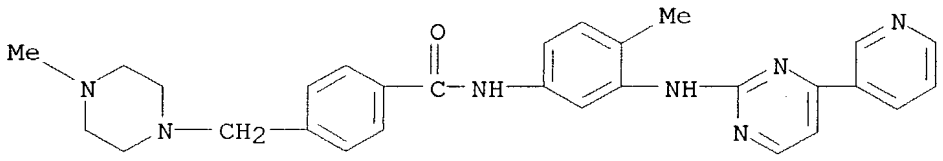
AB CGP 57148 is a compound of the 2-phenylaminopyrimidine class that selectively inhibits the tyrosine kinase activity of the ABL and the **platelet**-derived growth factor receptor (PDGFR) protein tyrosine kinases. We previously showed that CGP 57148 selectively kills p210BCR-ABL-expressing cells. To extend these observations, we evaluated the ability of CGP 57148 to inhibit other activated ABL tyrosine kinases, including p185BCR-ABL and TEL-ABL. In cell-based assays of ABL tyrosine phosphorylation, inhibition of ABL kinase activity was observed at concns. similar to that reported for p210BCR-ABL. Consistent with the in vitro profile of this compound, the growth of cells expressing activated ABL protein tyrosine kinases was inhibited in the absence of exogenous growth factor. Growth inhibition was also observed with a p185BCR-ABL-pos. acute lymphocytic leukemia (ALL) cell line generated from a Philadelphia chromosome-pos. ALL patient. As CGP 57148 inhibits the PDGFR kinase, we also showed that cells expressing an activated PDGFR tyrosine kinase, TEL-PDGFR, are sensitive to this compound Thus, this compound may be useful for the treatment of a variety of BCR-ABL-pos. leukemias and for treatment

of the subset of chronic myelomonocytic leukemia patients with a TEL-PDGFR fusion protein.

IT **152459-95-5**, CGP 57148
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of growth of cells expressing BCR-ABL, TEL-ABL, and TEL-PDGFR fusion proteins by tyrosine kinase inhibitor CGP 57148)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 33 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:123312 CAPLUS

DN 126:220297

TI Potent and selective inhibitors of the ABL-kinase: phenylaminopyrimidine (PAP) derivatives

AU Zimmermann, Jurg; Buchdunger, Elisabeth; Mett, Helmut; Meyer, Thomas; Lydon, Nicholas B.

CS Ciba Pharmaceuticals Division, Oncology Research Department, Ciba-Geigy Limited, Basel, CH-4002, Switz.

SO Bioorganic & Medicinal Chemistry Letters (1997), 7(2), 187-192
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier

DT Journal

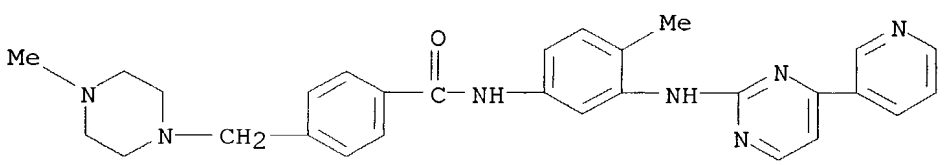
LA English

AB Due to its relatively clear etiol., chronic myelogenous leukemia (CML) represents an ideal disease target for a therapy using a selective inhibitor of the Bcr-Abl tyrosine protein kinase. Extensive optimization of the class of phenylamino-pyrimidines yielded highly potent and selective Bcr-Abl kinase inhibitors.

IT **152459-95-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylaminopyrimidine derivs. as inhibitors of ABL-kinase)

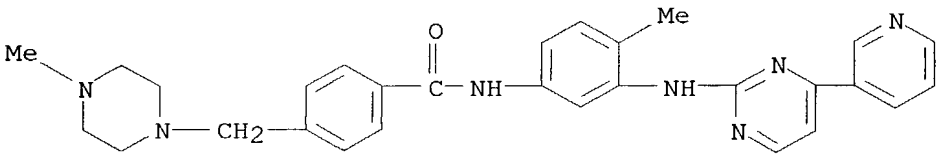
RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 34 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:22420 CAPLUS
DN 124:164458
TI Inhibition of the Abl protein-tyrosine kinase in vitro and in vivo by a 2-phenylaminopyrimidine derivative
AU Buchdunger, Elisabeth; Zimmermann, Juerg; Mett, Helmut; Meyer, Thomas; Mueller, Marcel; Druker, Brian J.; Lydon, Nicholas B.
CS Ciba Pharmaceuticals Division, Oncology Research Department, Ciba-Geigy Limited, Basel, CH-4002, Switz.
SO Cancer Research (1996), 56(1), 100-4
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB Oncogenic activation of Abl proteins due to structural modifications can occur as a result of viral transduction or chromosomal translocation. The tyrosine protein kinase activity of oncogenic Abl proteins is known to be essential for their transforming activity. Therefore, we have attempted to identify selective inhibitors of the Abl tyrosine protein kinase. Herein we describe an inhibitor (CGP 57148) of the Abl and **platelet**-derived growth factor (PDGF) receptor protein-tyrosine kinases from the 2-phenylaminopyrimidine class, which is highly active in vitro and in vivo. Submicromolar concns. of the compound inhibited both v-Abl and PDGF receptor autophosphorylation and PDGF-induced c-fos mRNA expression selectively in intact cells. In contrast, ligand-induced growth factor receptor autophosphorylation in response to epidermal growth factor (EGF), insulin-like growth factor-I, and insulin showed no or weak inhibition by high concns. of CGP 57148. C-fos mRNA expression induced by EGF, fibroblast growth factor, or phorbol ester was also insensitive to inhibition by CGP 57148. In antiproliferative assays, the compound was more than 30-100-fold more potent in inhibiting growth of v-abl-transformed PB-3c cells and v-sis-transformed BALB/c 3T3 cells relative to inhibition of EGF-dependent BaLB/MK cells, interleukin-3-dependent FDC-P1 cells, and the T24 bladder carcinoma line. Furthermore, anchorage-independent growth of v-abl- and v-sis-transformed BALB/c 3T3 cells was inhibited potently by CGP 57148. When tested in vivo, CGP 57148 showed antitumor activity at tolerated doses against tumorigenic v-Abl- and v-sis-transformed BALB/c 3T3 cells. In contrast, CGP 57148 had no antitumor activity when tested using src-transformed BALB/c 3T3 cells. These findings suggest that CGP 57148 may have therapeutic potential for the treatment of diseases that involve abnormal cellular proliferation induced by Abl protein-tyrosine kinase deregulation or PDGF receptor activation.
IT **152459-95-5**, CGP 57148
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in treatment of diseases that involve abnormal cellular proliferation induced by Abl protein-tyrosine kinase deregulation or PDGF receptor activation)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



L18 ANSWER 35 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:107056 CAPLUS
DN 120:107056
TI Preparation of 2-anilinopyrimidines as antiatherosclerotics and neoplasm inhibitors
IN Zimmermann, Juerg
PA Ciba-Geigy A.-G., Switz.
SO Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 564409	A1	19931006	EP 1993-810219	19930325
EP 564409	B1	20000119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
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AT 188964	E	20000215	AT 1993-810219	19930325
			CH 1992-1083 A	19920403
ES 2142857	T3	20000501	ES 1993-810219	19930325
			CH 1992-1083 A	19920403
PT 564409	T	20000630	PT 1993-810219	19930325
			CH 1992-1083 A	19920403
CA 2093203	AA	19931004	CA 1993-2093203	19930401
CA 2093203	C	20021126		
			CH 1992-1083 A	19920403
CZ 283944	B6	19980715	CZ 1993-560	19930401
			CH 1992-1083 A	19920403
RU 2125992	C1	19990210	RU 1993-5357	19930401
			CH 1992-1083 A	19920403
IL 105264	A1	19990411	IL 1993-105264	19930401
			CH 1992-1083 A	19920403
SK 280620	B6	20000516	SK 1993-280	19930401
			CH 1992-1083 A	19920403
NO 9301283	A	19931004	NO 1993-1283	19930402
			CH 1992-1083 A	19920403
ZA 9302397	A	19931004	ZA 1993-2397	19930402
			CH 1992-1083 A	19920403
AU 9335694	A1	19931007	AU 1993-35694	19930402
AU 666709	B2	19960222		
			CH 1992-1083 A	19920403
CN 1077713	A	19931027	CN 1993-103566	19930402
CN 1043531	B	19990602		
			CH 1992-1083 A	19920403
HU 64050	A2	19931129	HU 1993-982	19930402
			CH 1992-1083 A	19920403
JP 06087834	A2	19940329	JP 1993-78096	19930405
JP 2706682	B2	19980128		
			CH 1992-1083 A	19920403

	GR 3032927	T3	20000731	GR 2000-400623	20000310
				CH 1992-1083	A 19920403

PATENT FAMILY INFORMATION:

FAN 1995:735375

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9509852	A1	19950413	WO 1994-EP3149	19940921
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				CH 1994-2278	A 19940718
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				CH 1993-2966	A 19931001
				CH 1994-2278	A 19940718
	CA 2148477	AA	19950413	CA 1994-2148477	19940921
				CH 1993-2966	A 19931001
	AU 9476975	A1	19950501	AU 1994-76975	19940921
	AU 693804	B2	19980709		
				CH 1993-2966	A 19931001
				CH 1994-2278	A 19940718
				WO 1994-EP3149	W 19940921
	EP 672040	A1	19950920	EP 1994-927633	19940921
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
				CH 1993-2966	A 19931001
				CH 1994-2278	A 19940718
				WO 1994-EP3149	W 19940921
	JP 08504834	T2	19960528	JP 1994-510576	19940921
				CH 1993-2966	A 19931001
				CH 1994-2278	A 19940718
				WO 1994-EP3149	W 19940921

FAN 1996:380210

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5521184	A	19960528	US 1994-234889	19940428
				CH 1992-1083	A 19920403
				US 1993-42322	B219930402
				CH 1993-2966	A 19931001
	CA 2148477	AA	19950413	CA 1994-2148477	19940921
				CH 1993-2966	A 19931001

OS MARPAT 120:107056

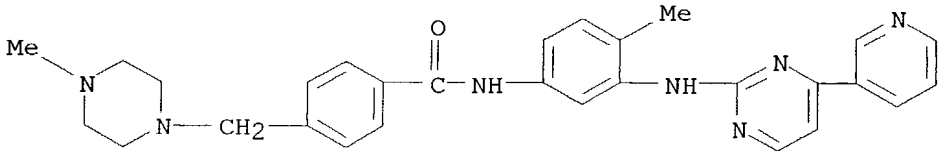
AB Title compds. [I; R1 = pyridyl, 4-pyrazinyl, (acyl)aminophenyl, etc.; R2, R3 = H, alkyl; 1 or 2 of R4-R8 = NO2, fluoroalkoxy, NR9C(:X)YnR10 and the others = H, alkyl, alkanoyl, CF3, etc.; R9 = H, alkyl; R10 = (cyclo)aliphatic group, heterocyclyl, aryl, etc.; X = O, S, NH, etc.; Y = O or NH; n = 0 or 1] were prepared Thus, 3-(O2N)C6H4NHC(:NH)NH2 [preparation from 3-(O2N)C6H4NH2 given] was cyclocondensed with R1COCH:CHNMe2 (R1 = 3-pyridyl) (preparation from 3-acetylpyridine given) to give I (R1 = 3-pyridyl, R2 = R3 = R5-R8 = H, R4 = NO2). I had IC50 of .apprx.0.5 to 5 μM against protein kinase C in vitro.

IT **152459-95-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antiatherosclerotic and neoplasm inhibitor)

RN 152459-95-5 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)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NEWS 4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 5	FEB 05	German (DE) application and patent publication number format changes
NEWS 6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 8	MAR 03	FRANCEPAT now available on STN
NEWS 9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS 10	MAR 29	WPIFV now available on STN
NEWS 11	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA
NEWS 12	APR 26	PROMT: New display field available
NEWS 13	APR 26	IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS 14	APR 26	LITALERT now available on STN
NEWS 15	APR 27	NLDB: New search and display fields available
NEWS 16	May 10	PROUSDDR now available on STN
NEWS 17	May 19	PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS 18	May 12	EXTEND option available in structure searching
NEWS 19	May 12	Polymer links for the POLYLINK command completed in REGISTRY

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
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NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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DICTIONARY FILE UPDATES:  16 MAY 2004  HIGHEST RN 682330-24-1

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http://www.cas.org/ONLINE/DBSS/registryss.html

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L1      STRUCTURE UPLOADED

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ENTER SCOPE OF SEARCH (SAMPLE), FULL, RANGE, OR SUBSET:full
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FULL SCREEN SEARCH COMPLETED -   2088 TO ITERATE

100.0% PROCESSED    2088 ITERATIONS                          8 ANSWERS
SEARCH TIME: 00.00.01

L2            8 SEA SSS FUL L1

=> s restenosis
L3            0 RESTENOSIS

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                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       159.85     160.06

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FILE COVERS 1907 - 17 May 2004 VOL 140 ISS 21
FILE LAST UPDATED: 16 May 2004 (20040516/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s restenosis
L5         5528 RESTENOSIS

=> s stent
L6         1886 STENT

=> s l5 or l6
L7         6753 L5 OR L6

=> s l4 and l7
L8            7 L4 AND L7

=> d l8 fbib ab hitstr 1-7

L8   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:80546  CAPLUS
DN   140:133897
TI   Medical devices comprising a protein-tyrosine kinase inhibitor to inhibit
     restenosis
IN   Tremble, Patrice; Carlyle, Wenda
PA   Medtronic Ave Inc., USA
SO   PCT Int. Appl., 35 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
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PI   WO 2004009147       A1   20040129      WO 2003-US22546  20030717
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-397149PP 20020718

AB Implantable medical devices having an anti-restenotic coatings are disclosed. Specifically, implantable medical devices having coatings of protein-tyrosine kinase inhibitors are disclosed. The anti-restenotic protein-tyrosine kinase inhibitor is imatinib mesylate and its pharmaceutically acceptable derivs. The anti-restenotic medial devices include stents, catheters, microparticles, probes and vascular grafts. The medical devices can be coated using any method known in the art including compounding the protein-tyrosine kinase inhibitor with a biocompatible polymer, e.g., polycaprolactone, prior to applying the coating. Moreover, medical devices composed entirely of biocompatible polymer-protein-tyrosine kinase inhibitor blends are disclosed. Addnl., medical devices having a coating comprising at least one protein-tyrosine kinase inhibitor in combination with at least one addnl. therapeutic agent, such as an antiplatelet agent, antifibrotic agent, proliferation inhibitor, or anti-inflammatory agent, are also disclosed. Furthermore, related methods of using and making the anti-restenotic implantable devices are also disclosed.

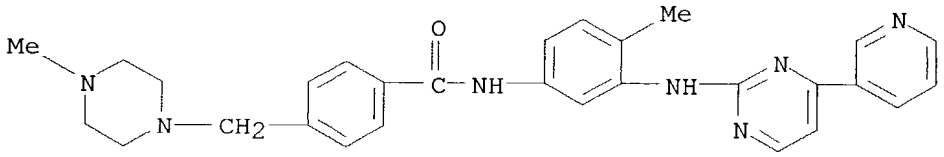
IT **220127-57-1**, Imatinib mesylate
RL: DEV (Device component use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable devices coated with protein-tyrosine kinase inhibitor for drug controlled release and inhibition of **restenosis**)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

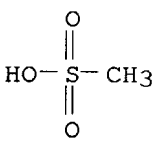
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:836920 CAPLUS
DN 139:328378
TI Drug eluting vascular **stent** and method of treating hyperproliferative vascular disease
IN Moussa, Issam
PA USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086497	A1	20031023	WO 2003-IB1230	20030404

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-373107PP 20020416

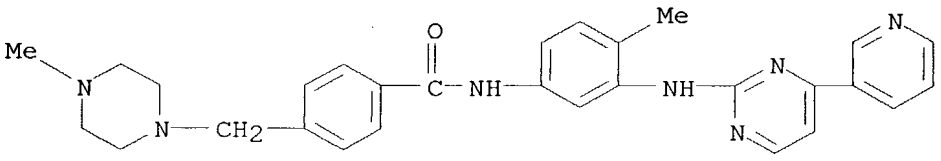
AB This invention provides a drug eluting vascular **stent** and a method of preventing or treating hyperproliferative vascular disease in a mammal by administering an antiproliferative effective amount of imatinib mesylate, alone or in combination with other compds., via a vascular **stent**. The hyperproliferative vascular disease may be caused by vascular injury, percutaneous transluminal coronary angioplasty,etc.

IT **220127-57-1**, Imatinib mesylate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug eluting vascular **stent** and method of treating hyperproliferative vascular disease)

RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

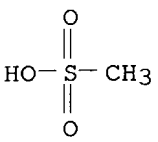
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

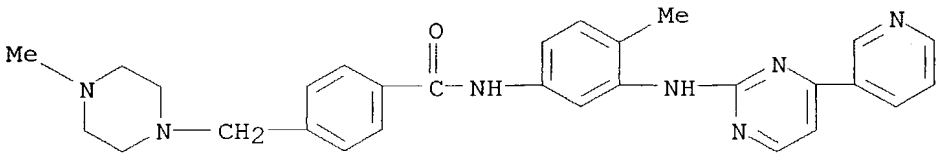
L8 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:696780 CAPLUS
DN 139:219397
TI N-{5-[4-(4-methyl-piperazino-methyl)-benzoylamido]-2-methylphenyl}-4-(3-pyridyl)-2-pyrimidine-amine coated stents
IN Prescott, Margaret Forney; Feldman, David Louis
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003072159	A1	20030904	WO 2003-EP2028	20030227

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR

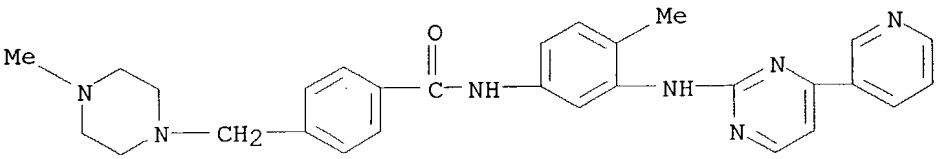
US 2002-360254PP 20020228

AB The invention relates to the local administration of N-{5-[4-(4-methyl-piperazino-methyl)-benzoylamido]-2-methylphenyl}-4-(3-pyridyl)-2-pyrimidine-amine (I) or a pharmaceutically acceptable salt or crystal form thereof, optionally in conjunction with one or more other active ingredients, and a device adapted for such local administration. I significantly reduced neointimal lesion formation in rats at 28 days following balloon injury when administered at a dose of 0.2-3.5 mg/kg.
IT **152459-95-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(piperazino-methylbenzoylamido pyridylpyrimidineamine coated stents)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:639686 CAPLUS
DN 140:139030
TI Leflunomide analogue FK778 is vasculoprotective independent of its immunosuppressive effect: potential applications for **restenosis** and chronic rejection
AU Savikko, Johanna; von Willebrand, Eva; Haeyry, Pekka
CS Transplantation Laboratory, Haartman Institute, Helsinki Univ. Central Hospital, Helsinki, Finland
SO Transplantation (2003), 76(3), 455-458
CODEN: TRPLAU; ISSN: 0041-1337
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB BACKGROUND: Leflunomide (LFM) inhibits exptl. both acute and chronic allograft rejection. The inhibition of dihydroorotate dehydrogenase (DHODH) in pyrimidine synthesis is suggested to be the major immunosuppressive mechanism. The mechanism of its vasculoprotective effect is not known, although it may be linked to inhibition of receptor tyrosine kinases (RTK). Here, we have investigated whether sufficient vasculoprotective effect could be obtained upon administration of FK778, a LFM analog with shorter half-life, and compared the dose response with that of a known platelet-derived growth factor RTK inhibitor, imatinib, after endothelial injury in vivo. METHODS AND RESULTS: Wistar rats were used for aorta denudations. The rats remained untreated or received either FK778 or imatinib (STI571) at decreasing oral doses from 10 mg/kg per day. Half of the animals in both treatment groups also received uridine to reverse DHODH activity. Morphometric anal. was done after 14 day follow-up. In the untreated group, moderate neointima formation was detected. FK778 almost completely inhibited intimal formation, with or without uridine addition ($P<0.05$). Imatinib also inhibited neointima formation ($P<0.05$), whereas exogenous uridine reversed its effect. CONCLUSIONS: Our results demonstrate that FK778 inhibits neointima formation by way of a mechanism that is independent of DHODH inhibitory activity on vascular smooth muscle cell. Interestingly, the effect of imatinib was inhibited by uridine, suggesting that part of its action on vascular stenosis could be mediated through inhibition of pyrimidine synthesis.
IT **152459-95-5**, Imatinib
RL: PAC (Pharmacological activity); BIOL (Biological study)
(leflunomide analog FK778 is vasculoprotective independent of its immunosuppressive effect in relation to imatinib)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:610603 CAPLUS
DN 139:159912
TI Sequences of mouse and human protein SUAP (small ubiquinated apoptotic protein) and uses in inducing growth arrest and apoptosis in cancer cells
IN Baker, Stacey Jill; Reddy, E. Premkumar
PA Temple University - of the Commonwealth System of Higher Education, USA
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003064616	A2	20030807	WO 2003-US2942	20030131

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-353622PP 20020131

AB Growth arrest and apoptosis in cells can be induced in cells which are resistant to apoptosis with SUAP (small ubiquinated apoptotic protein) and derivs., homologs and analogs of SUAP. Detection of endogenous SUAP expression can also be used as a marker of apoptosis in cells undergoing apoptosis-inducing therapeutic treatments. The invention provides protein and cDNA sequences of mouse and human protein SUAP (small ubiquinated apoptotic protein). SUAP RNA was highly expressed in multiple tissues, including heart, brain, testis, liver and kidney. SUAP expression was also observed in lung and spleen, albeit to a lesser extent. Endogenous SUAP was unstable and was subject to degradation by proteosome. SUAP was up-regulated during G-CSF-induced terminal differentiation of 32Dcl3 cells and IL-3 withdrawal-induced apoptosis of 32Dcl3. SUAP RNA was induced in MCF7 cells in response to serum-withdrawal-induced apoptosis; taxol-induced apoptosis; etoposide-induced apoptosis; cisplatin-induced apoptosis. SUAP RNA was induced in response to irradiation of DU145 and LnCap prostate tumor cells; androgen ablation of LnCap cells; and irradiation of androgen depleted LnCap cells.

IT **220127-57-1**, STI571
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as external apoptosis inducing-stimulus; sequences of mouse and human

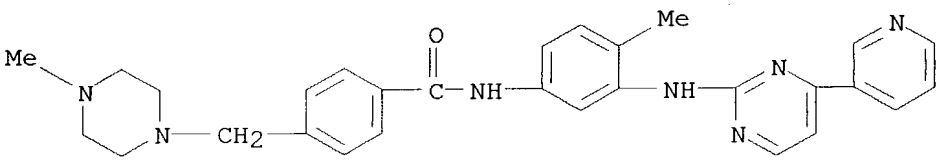
protein SUAP (small ubiquinated apoptotic protein) and uses in inducing growth arrest and apoptosis in cancer cells)

RN 220127-57-1 CAPLUS

CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

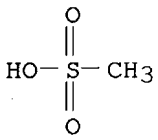
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



CM 2

CRN 75-75-2
CMF C H4 O3 S



L8 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:413877 CAPLUS

DN 138:396218

TI Combination for the treatment of endothelial damage

IN Alitalo, Kari; Heldin, Carl Henrik; Leppanen, Olli; Ostman, Arne; Yla-Herttuala, Seppo

PA Finland

SO U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

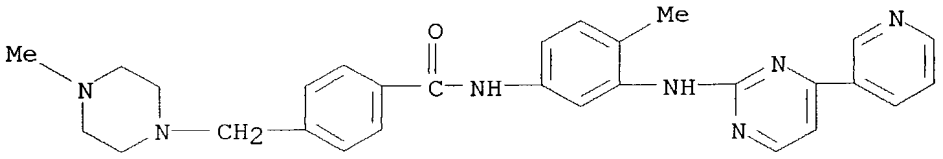
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003099687	A1	20030529	US 2002-227081	20020823
				GB 2001-20690 A	20010824

AB The invention relates to a combination of (a) an inhibitor of platelet-derived growth factor (PDGF) activity and (b) a vector for vascular endothelial growth factor (VEGF-, especially VEGF-C) gene transfer, a pharmaceutical preparation comprising (a) and (b) in combination together with a pharmaceutically acceptable carrier material; a product comprising (a) and (b) as defined above and optionally a pharmaceutically acceptable carrier material, for simultaneous, chronol. staggered or sep. use; a

method of administering or the use of said combination or product for the treatment of endothelial damage; and/or to the use of (a) and (b) for the manufacture of said pharmaceutical preparation or product for the treatment of endothelial damage.

IT **152459-95-5 220127-57-1,** STI571
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination for treatment of vascular endothelial damage using platelet-derived growth factor inhibitors and gene transfer of vascular endothelial growth factor in relation to formulation and pharmacokinetics)

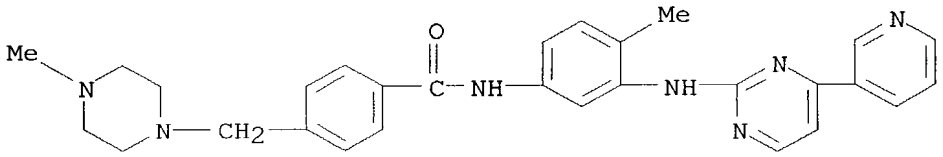
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RN 220127-57-1 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

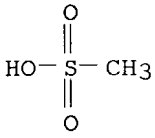
CM 1

CRN 152459-95-5
CMF C29 H31 N7 O



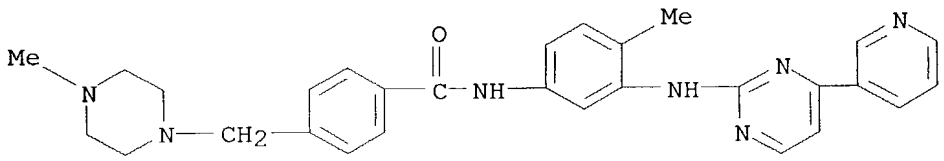
CM 2

CRN 75-75-2
CMF C H4 O3 S



L8 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:413549 CAPLUS
DN 131:223278
TI Selective tyrosine kinase inhibitor for the platelet-derived growth factor receptor in vitro inhibits smooth muscle cell proliferation after reinjury of arterial intima in vivo
AU Myllarniemi, Marjukka; Frosen, Juhana; Ramirez, Lazaro G. Calderon; Buchdunger, Elisabeth; Lemstrom, Karl; Hayry, Pekka
CS Transplantation Laboratory, University of Helsinki, Helsinki, FIN-00014, Finland
SO Cardiovascular Drugs and Therapy (1999), 13(2), 159-168
CODEN: CDTHET; ISSN: 0920-3206
PB Kluwer Academic Publishers
DT Journal
LA English
AB The long-term success of coronary angioplasty is limited by **restenosis.** This study was undertaken to investigate whether and to what extent the enhanced proliferative response observed in a balloon reinjury model of rat aorta is regulated by the PDGF receptor (PDGF-R). Balloon injury was performed to 14-day-old pre-existing neointimal lesion in rat aorta. PDGF receptor and ligand immunoreactivity were measured at several time points after the first and second injury, and PDGF-R signaling was blocked with a selective inhibitor of PDGF-R tyrosine kinase. In the neointima, after repeated injury, upregulation of PDGF-AA was seen to coincide with a prompt proliferative response of smooth muscle cells (SMC). Administration of the PDGF-R tyrosine kinase inhibitor in vivo, tested and found to inhibit the proliferation of SMC induced by PDGF-AA and PDGF-BB, but not by IGF-1, EGF, or bFGF, resulted in a 60% reduction in the absolute number and percentage of BrdU + cells after the second balloon injury to pre-existing neointima, but had no significant effect on proliferation after the first injury. Endpoint lesion area was reduced by 50% in the treated group at 14 days after the second injury. The results suggest that systemic administration of a tyrosine kinase inhibitor specific for the PDGF-R can be useful in the prevention of **restenosis.**
IT **152459-95-5**, CGP 57148B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(tyrosine kinase inhibitor for PDGF receptor inhibits smooth muscle cell proliferation after reinjury of arterial intima)
RN 152459-95-5 CAPLUS
CN Benzamide, 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT